WEST

Generate Collection

L1: Entry 6 of 12 File: JPAB Sep 5, 2000

PUB-NO: JP02000236835A
DOCUMENT-IDENTIFIER: JP 2000236835 A
TITLE: FOOD PREPARED BY USING KOTO-SUGI AS MAIN RAW MATERIAL AND ITS PREPARATION

PUBN-DATE: September 5, 2000

INVENTOR-INFORMATION:

NAME	COUNTRY
HIYO, SEKI	
EN, SEIKA	

ASSIGNEE-INFORMATION:

NAME	COUNTRY
EN SEIKA	
HIYO SEKI	

APPL-NO: JP11078237
APPL-DATE: February 17, 1999

INT-CL (IPC): A23L 1/212; A23L 1/30; A61P 35/00; A61K 35/78

ABSTRACT:

PROBLEM TO BE SOLVED: To obtain a food produced by using Koto-sugi (a tree of the family Taxaceae, native to Yunnan Province, China, or the like) as a main raw material and incorporated with Seiyo-ninjin (rhizome of Vitex agnus-castus), or the like, believed to be good for health, especially for the prevention of cancer.

SOLUTION: The trunk (or leaf or twig) of Koto-sugi is powdered to 20-60

WEST

End of Result Set

☐ Generate Collection

L1: Entry 12 of 12 File: DWPI Dec 9, 1987

DERWENT-ACC-NO: 1987-343204
DERWENT-WEEK: 198749

TITLE: Dopaminergic medicaments - contain extract of Vitex agnus-castus

INVENTOR: POPP, H O

PATENT-ASSIGNEE:

ASSIGNEE	CODE
APOTHEKER POPP OHG	APOTN

PRIORITY-DATA: 1986DE-3618627 (June 3, 1986)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 248215 A	December 9, 1987	G	007	
DE 3618627 A	December 10, 1987		000	
DE 3618627 C	February 6, 1992		000	
DE 3786425 G	August 12, 1993		000	A61K035/78
EP 248215 B1	July 7, 1993	G	007	A61K035/78

DESIGNATED-STATES: AT BE CH DE FR GB IT LI LU NL SE AT BE CH DE FR GB IT LI LU NL SE

CITED-DOCUMENTS:4.Jnl.Ref; A3...8940 ; No-SR.Pub

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
EP 248215A	May 2, 1987	1987EP-0106390	
DE 3618627A	June 3, 1986	1986DE-3618627	
DE 3786425G	May 2, 1987	1987DE-3786425	
DE 3786425G	May 2, 1987	1987EP-0106390	
DE 3786425G		EP 248215	Based on
EP 248215B1	May 2, 1987	1987EP-0106390	

INT-CL (IPC): A61K 35/78

ABSTRACTED-PUB-NO: EP 248215A
BASIC-ABSTRACT:

Dopaminergic medicaments for treating diseases caused or influenced by dopamine deficiency contain an extract of Vitex agnus-castus.

The extract is pref. an alcohol extract of Vitex fruits. The medicaments may be administered orally.

USE - The medicaments are esp. useful as prolactin inhibitors for treating

premenstrual syndrome, mastodynia, mastopathy, bleeding disorders, infertility and amenorrhoea in females, and loss of libido and potency, infertility and acne in males.
ABSTRACTED-PUB-NO:

EP 248215B
EQUIVALENT-ABSTRACTS:

Dopaminergic medicaments for treating diseases caused or influenced by dopamine deficiency contain an extract of Vitex agnus-castus.

The extract is pref. an alcohol extract of Vitex fruits. The medicaments may be administered orally.

USE - The medicaments are esp. useful as prolactin inhibitors for treating premenstrual syndrome, mastodynia, mastopathy, bleeding disorders, infertility and amenorrhoea in females, and loss of libido and potency, infertility and acne in males.

DE 3618627C

Use of extracts of the plant vitex agnus castus is claimed for treating hyperprolactinaemia.

USE/ADVANTAGE - For treating Parkinson's disease, and also premenstrual syndrome, mastodymia, mastopathy, blood disorders, infertility and amenorrhoea in women and loss of libido and potency, infertility and acne in men. Known treatment with dopamine antagonists leads to undesired side effects such as nausea, vomiting, dizziness, hallucinati on, dyskinesia etc. (6pp)

CHOSEN-DRAWING: Dwg.0/2 Dwg.0/2

TITLE-TERMS: DOPAMINERGIC MEDICAMENT CONTAIN EXTRACT

DERWENT-CLASS: B04

CPI-CODES: B04-A07F2; B12-A07; B12-E09; B12-G01A; B12-H04;

CHEMICAL-CODES:

Chemical Indexing M1 *01*
Fragmentation Code
M423 M781 M903 P617 P943 V400 V406
Registry Numbers
87140 1286M

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C1987-146510

WEST

☐ Generate Collection

L1: Entry 4 of 12 File: USPT Sep 5, 2000

DOCUMENT-IDENTIFIER: US 6113907 A
TITLE: Pharmaceutical grade St. John's Wort

BSPR:
By way of illustrative example, but not by way of limitation, pharmaceutical grade St. John's Wort may be combined with a pharmaceutical grade botanical material such as V. agnus-castus, valerian, kava, skullcap or echinacea. For V. agnus-castus, see U.S. patent application Ser. No. 08/955,410, entitled "PHARMACEUTICAL GRADE VITEX AGNUS CASTUS", filed concurrently, incorporated in its entirety by reference herein. For valerian, see U.S. patent application Ser. No. 08/956,615, entitled "PHARMACEUTICAL GRADE VALERIAN", filed concurrently, incorporated in its entirety by reference herein. For kava, see U.S. patent application Ser. No. 08/838,198, entitled "PHARMACEUTICAL GRADE BOTANICAL DRUGS", filed Apr. 15, 1997, chapter 28, pages 173-175, incorporated in its entirety by reference herein.

See also
6264995

WEST

Generate Collection

L1: Entry 3 of 12 File: USPT Sep 12, 2000

DOCUMENT-IDENTIFIER: US 6117429 A
TITLE: Compositions and treatments for reducing potential unwanted side effects associated with long-term administration of androgenic testosterone precursors

ORPL:
Saden-Krehula, M., Kustrak, D., and Balzevid, N. .increment..sup.4
-3-Ketosteroids in Flowers and Leaves of Vitex agnus-castus. Acta Pharm. Jugosl. vol. 41 (1991) 237-241.

WEST

Generate Collection

L1: Entry 2 of 12 File: USPT Apr 3, 2001

DOCUMENT-IDENTIFIER: US 6210738 B1
TITLE: Freeze-dried ginseng berry tea

DEPR:
A generalized formula for the tea beverage of the present invention comprises ginseng berry combined with fruit extract and/or one or more natural health promoting ingredients. Natural health promoting ingredients may include, for example and not by way of limitation, agnus castus (Vitex agnus-castus), agrimony (Agrimonia eupatoria), anise (Pimpinella anisum), arjuna (Terminalia arjuna), arnica (Arnica montana), asafoetida (Ferula assa-foetida), astragalus (Astragalus membranaceus), avens (Geum urbanum), bay laurel (Laurus nobilis), Beleric myrobalan (Terminalia belerica), betony (Stachys officinalis), bilberry (Vaccinium myritillus), bistort (Polygonum bistorta), black cohosh (Cimicifuga racemosa), blackcurrant (Ribes nigrum), black haw (Viburnum prunifolium), bogbean (Menyanthes trifoliata), boldo (Peumus boldus), boneset (Eupatorium perfoliatum), buchu (Barosma betulina), bugleweed (Lycopus virginicus), burdock (Arctium lappa), calendula (Calendula officinalis), calumba (Jateorhiza palmata), cardamom (Eletteria cardamomum), cayenne (Capsicum frutescens), cerasee (Momordica charantia), chiretta (Swertia chirata), cinchona (cinchona), cinnamon (Cinnamomum verum), clove (Eugenia caryophyllata), codonopsis (Codonopsis pilosula), coltsfoot (Tussilago farfara), comfrey (Symphytum officinale), common plantain (Plantago major), cornsilk (Zea mays), cowslip (Primula veris), crampbark (Viburnum opulus), damiana (Turnera diffusa), dandelion (Taraxacum officinale), devil's claw (Harpagophytum procumbens), echinacea (Echinacea spp.), eggplant (Solanum melongena), elder (Sambucus nigra), elecampane (Inula helenium), ephedra (Ephedra sinica), eucalyptus (Eucalyptus globulus), evodia (Evodia rutaecarpa), evening primrose (Oenothera biennis), eyebright (euphrasia spp.), fennel (Foeniculum vulgare), fumitory (Fumaria officinalis), galangal (Alpinia officinarum), garlic (Allium sativum), gentian (Gentiana lutea), ginger (Zingiber officinale), ginkgo (Ginkgo biloba), goat's rue (Galega officinalis), goldenrod (Solidago vigaurea), hanbane (Hyoscyamus niger), hops (Humulus lupulus), horsemint (Monarda punctata), Indian gooseberry (Emblica officinalis), jamaica dogwood (Piscidia erythrina), java tea (Orthosiphon aristata), jujube (Ziziphus jujuba), kantakari (Solanum xanthocarpum), lavender (Lavandula officinalis), lapacho (Tabebuia spp.), lemon (Citrus limon), lemon balm (Melissa officinalis), licorice (Glycyrrhiza glabra), linden (tilia), lobelia (Lobelia inflata), lycium (Lycium chinense), manioc (Manihot esculenta), meadowsweet (Filipendula ulmaria), milk thistle (Carduus marianus), Muira puama (Liriosma ovata), mullein (Verbascum thapsus), myrrh (Commiphora molmol), nettle (Uritica dioica), oats (Avena sativa), passionflower (Passiflora incarnata), patchouli (Pogostemon cablin), picrorrhiza (Picrorrhiza kurroa), prickly ash (Zanthoxylum americanum), purslane (Protulaca oleracea), rehmannia (Rehmannia glutinosa), rosemary (Rosmarinus officinalis), sarsaparilla (smilax spp.), schisandra (Schisandra chinensis), skullcap (Scutellaria lateriflora), slippery elm (Ulmus rubra), soapwort (Saponaria officinalis), spiny restharrow (Ononis spinosa), squaw vine (Mitchella repens), sweet basil (Ocimum basilicum), tea tree (Melaleuca alternifolia), tree lungwort (Lobaria pulmonaria), turmeric (Curcuma longa), thyme (Thymus vulgaris), vervain (Verbena officinalis), white willow (Salix alba), winter cherry (Physalis alkekengi), withania (Withania somnifera), wormwood (Artemisia absinthium), yarrow (Achillea millefolium), yellow dock (Rumex crispus) as well as vitamins, minerals and amino acids. The forrnula may also contain other ingredients to promote health or adjust flavor.

CLPR:
6. The composition of claim 1 wherein said one or more natural health promoting ingredients comprises an ingredient selected from the group consisting of agnus castus (Vitex agnus-castus), agrimony (Agrimonia eupatoria), anise (Pimpinella anisum), arjuna (Terminalia arjuna), arnica (Arnica montana), asafoetida (Ferula assa-foetida), astragalus (Astragalus menmbranaceus), avens (Geum urbanum), bay laurel (Laurus nobilis), Beleric myrobalan (Terminalia belerica), betony (Stachys officinalis), bilberry (Vaccinium myritillus), bistort (Polygonum bistorta), black cohosh (Cimicifuga racemosa), blackcurrant (Ribes nigrum), black haw (Viburnum prunifolium), bogbean (Menyanthes trifoliata), boldo (Peumus boldus), boneset (Eupatorium perfoliatum), buchu (Barosma betulina), bugleweed (Lycopus virginicus), burdock (Arctium lappa), calendula (Calendula officinalis), calumba (Jateorhiza palmata), cardamom (Eletteria cardamomum), cayenne (Capsicum frutescens), cerasee (Momordica charantia), chiretta (Swertia chirata), cinchona (cinchona), cinnamon (Cinnamomum verum), clove (Eugenia caryophyllata), codonopsis (Codonopsis pilosula), coltsfoot (Tussilago farfara), comfrey (Symphytum officinale), common plantain (Plantago major), cornsilk (Zea mays), cowslip (Primula veris), crampbark (Viburnum opulus), damiana (Turnera diffusa), dandelion (Taraxacum officinale), devil's claw (Harpagophytum procumbens), echinacea (Echinacea spp), eggplant (Solanum melongena), elder (Sambucus nigra), elecampane (Inula helenium), ephedra (Ephedra sinica), eucalyptus (Eucalyptus globulus), evodia (Evodia rutaecarpa), evening primrose (Oenothera biennis), eyebright (euphrasia spp.), fennel (Foeniculum vulgare), fumitory (Fumaria officinalis), galangal (Alpinia officinarum), garlic (Allium sativum), gentian (Gentiana lutea), ginger (Zingiber officinale), ginkgo (Ginkgo biloba), goat's rue (Galega officinalis), goldenrod (Solidago vigaurea), hanbane (Hyoscyamus niger), hops (Humulus lupulus), horsemint (Monarda punctata), Indian gooseberry (Emblica officinalis), jamaica dogwood (Piscidia erythrina), java tea (Orthosiphon aristata), jujube (Ziziphus jujuba), kantakari (Solanum xanthocarpum), lavender (Lavandula officinalis), lapacho (tabebuia spp.), lemon (Citrus limon), lemon balm (Melissa officinalis), licorice (Glycyrrthiza glabra), linden (tilia), lobelia (Lobelia inflata), lycium (Lycium chinense), manioc (Manihot esculenta), meadowsweet (Filipendula ulmaria), milk thistle (Carduus marianus), Muira puama (Liriosma ovata), mullein (Verbascum thapsus), myrrh (Commiphora molmol), nettle (Uritica dioica), oats (Avena sativa), passionflower (Passiflora incarnata), patchouli (Pogostemon cablin), picrorrhiza (Picrorrhiza kurroa), prickly ash (Zanthoxylum americanum), purslane (protulaca oleracea), rehmannia (Rehmannia glutinosa), rosemary (Rosmarinus officinalis), sarsaparilla (smilax spp.), schisandra (Schisandra chinensis), skullcap (Scutellaria lateriflora), slippery elm (Ulmus rubra), soapwort (Saponaria officinalis), spiny restharrow (Ononis spinosa), squaw vine (Mitchella repens), sweet basil (Ocimum basilicum), tea tree (Melaleuca alternifolia), tree lungwort (Lobaria pulmonaria), turmeric (Curcuma longa), thyme (Thymus vulgaris), vervain (Verbena officinalis), white willow (Salix alba), winter cherry (Physalis alkekengi), withania (Withania somnifera), wormwood (Artemisia absinthium), yarrow (Achillea millefolium), and yellow dock (Rumex crispus).

WEST

Generate Collection

L1: Entry 5 of 12 File: USPT May 25, 1999

DOCUMENT-IDENTIFIER: US 5906825 A
TITLE: Polymers containing antimicrobial agents and methods for making and using same

DEPR:
It should be understood that the present invention is broadly drafted, in one embodiment, towards incorporating phytochemicals as biocidal agents into polymeric materials. In several preferred embodiments of the present invention, capsicum, citric acid extract, and grapefruit seed extract may be used as biocidal agents. The present invention, however, encompasses the use of many other biocidal agents. The following, although illustrative of other examples of phytochemicals that can be incorporated as biocides, is not meant to be an all-inclusive list: Jasonia candicans (sesquiterpenes, lactones); Polygonum flaccidum (flavone and alpha santalene derivatives); Acalypha wikesiana (extracts); Pavetta owariensis (procyanidins); Plectranthus hereroensis (diterpenoids, diterpenes); Moss (Dicranin extract); Cannabis sativa (extract); Gloiosiphonia spp. (gloiosiphones); Laminaceae spp. (extract); Securidaca spp. (extract); Veronia spp. (extract); Hyptis umbrose (umbrosone); Asclepias syriaca (milkweed extract); Tagetes tenuifolia (thiophene); Calophyllum inophylloide (flavonoids); Tanacetum densum (sesquiterpene lactones, triterpenoids); Neorautanenia mitis (extract); Premna schimper (diterpene); Premna oligotricha (sesquiterpenes); Premna oligotricha (diterpenes); Jasonia candicans (essential oils); Visnea mocanera (beta-sitosterol, triterpenic betulinic acid, ursolic acid, plantanic acid); Asteraceae spp. (terthiophenes and polyynes); Petalostemum purpureum (extract); Camelia sinensis (catechin); Helichrysum picardii (flavonoids); Helichrysum italicum (flavonoids); Corydalis pallida (protoberberine alkloids); Shiraia bambusicola (perylenequinones); Fraxinum omus (hydroxycoumarins); Podocarpus nagi (totarol and nortiterpene dilactones); Heterotheca inuloides (sesquiterpenoids); Pelargonium spp. (essential oils); Piper sarmentosum (phenylpropanoids); Allium spp. (extract); Juniperus procera (diterpenes); Achillea conferta (flavonoids, flavones, sesquiterpenoid lactones); Magnolia virginiana (lignans, neolignans); Eucalyptus euglobal (euglobal); Armillaria mellea (armillaric acid); Dracena mannii (spirostanol saponin); Piper aduncum (chromenes, prenylated benzoic acid); Rhamnaceae spp. (cyclopeptide alkaloids); Buddleja globosa (verbascoside); Cephalocereus senilis (phytoalexin aurone); Salvia albocaerulea (diterpene); Gomphrena martiana and Gomphrena boliviana (extracts); Paepalanthus spp. (vioxanthin); Helichrysum stoechas and Helichrysum crispum (extracts); Achillea ptarmica (trans-pinocarveyl hydroperoxides); Dehaasia incrassata (alkaloids); Asteraceae spp. (extracts); Arctotis auriculate (extracts); Eriocephalus africanus (extracts): Felicia erigeroides (extracts); Hemerocallis fulva (phytosterols, fatty acid esters); Psoralea juncea (plicatin B); Pluchea symphytifolia (caffeic acid esters); Tovomitopsis psychotrifolia (Vitamin E derivative), Celosia argentea (triterpenoid saponins and flavonoids); Azadirachta indica (tetranortriterpenoid, mahmoodin, protolimonoids, naheedin); Moraceae spp. (coumarins); Hypericum erectum (phloroglucinol derivatives); Podospora appendiculate (Appenolides A, B, & C, furanones); Artemisia princeps var. orientalis, Artemisia capillaris, Artemisia mexicana and Artemisia scoparia (extract); Paddy malt (mash extract); Kigelia pinnata (extract); Acalypha wilkesiana (extract); seaweeds, seagrass and lemongrass (essential oils); Borrieria latifolia, Borreria setidens, Hedyotis diffusa), Hedyotis nudicaulis, Morinda elliptica, Morinda umbellata, Sida rhombifolia, and Vitex ovata (extracts); Tabebuia impetiginosa, Achyrocline spp., Larrea divaricata, Rosa borboniana, Punica granatum, Psidium guineense, Lithrea ternifolia (extracts);

Lepechinia caulescens, Lepidium virginicum and Tanacetum parthenium (extracts); Talaromyces flavus (extracts); Daucus carota (extract); Flabellia petiolata, Caulerpa prolifera, Halimeda tuna, Corallina elongata, Lithophyllum lichenoides, Phyllophora crispa, Cystoseira spp., Halopteris spp., Codium spp., Valonia utricularis, Posidonia oceanica, Zostera noltil and Cymodocea nodosa (extracts); Centauraea orientalis, Diospyros khaki, Sida hermaphrodita, Forsythia intermedia, Scutellaria polydon, Eugenia malaccensis and Eugenia jambolana (extracts); Fritillaria L. spp. (ebeinone, steroidal alkaloids); Kigelia pinnata, Peperomia pellucida, Populus nigra, Populus balsamifera and Populus deltoides (extracts); Melaleuca alternifolia (essential oil); Elfvingia applanata (naringenin); Ficus sycomorus, grapefruit seed, Garlic, Allicin, Peat, Strophanthus hispidus, Secamone afzeli, Mitracarpus scaberi, Entada abyssinjca, Terminalia spinosa, Harrisonia abyssinica, Ximinea caffra, Azadirachta indica, Spilanthes mauritiana, Terminalia spinosa (extracts); Cyanobacteria (ambigols A and B, tjipanazole); coffee (extract); Sporochnus pedunculatus, Dalbergia melanozylon, Celastrus scandens, Juglans nigra, Kalmia latifolia, Pelargonium xhortorum, Rhus glabra and Lindera benzoin (extracts); Striga densiflora, Striga orobanchioides, Striga lutea, Pistacia lentiscus L., Mitracarpus villosus, Bixa orellana, Bridelia ferruginea, Alpinia katsumadai, Alpinia officinarum, Artemisia capillaris, Casia obtusifolia, Dendrobium moniliforme, Epimedium grandiflorum, Glycyrrhiza glabra, Lithosperum erythrorhizon, Magnolia obovata, Morus bonbycis, Natopterygii incisium, Polygonum multiflorum, Prunus mume, Rheum palmatum, Ricinus communis, Sophora flavescens, Swertia japonica, black pepper, rosemary, red pepper, Isopyrum thalictroides, Calotropis procera, Chrysanthemum spp., Holarrhena antidysenterica, Lunularia crusiata, Dumertiera hirsuta, Exormotheca tuberifera, and liverwort (extracts); Filipendula ulmaria, Salix glauca, Usnea filipendula, Clkadina arbuscula (salicylic compounds); Tanacetum parthenium, Thymus capitatus, and Elfingia applanata (extracts); Fraxinus ornus (hydroxycoumarins, esculin, esculetin, fraxin, and fraxetin); Zizyphus nummularia, LONGO VITAL, Pelargonium spp., Scaevola sericea, Psychotria hawaiiensis, Pipturus albidis, Aleurites moluccana, Solanum niger, Piper methysticum, Barringtonia asiatica, Adansonia digitata, Harungana madagascariensis, Jacaranda mimosaefolia, Erythroxylum catauba, Bidens pilosa, Lemna minor, Potamogeton spp., Nasturtium officinale, Apium nodiflorum, Agaricus subrutilescens, Amanita virosa, Amanita pantherina, Lycoperdon perlatum, Psidium guajava, Averrhoa carambola, musa sapientum, Carica papaya, Passiflora edulis, Lansium domesticum and Baccaurea motleyana (extracts); horse radish, celandine grass, bur marigold and yarrow grass (extracts); Abuta grandifola, Cyperus articulatus, Gnaphalium spicatum, Pothomorphe peltata, Ficus sycomorus, Ficus Benjamina, Ficus bengalensis, Ficus religiosa, Alchornea cordifolia, Bridelia feruginea, Eucalyptus citriodora, Hymenocardia acida, Maprounea africana, Monachora arbuscula, Tedania ignis, Arenosclera spp., Amphimedon viridis, Polymastia janeirensis, Aplysina fulva, Pseudaxinella lunaecharta, Nelumbium speciosum and Mycale arenosa (extracts); cloves (eugenol acetate and iso-eugenol); Chrysthanemum boreale (sesquiterpenoid lactones); Eucalyptus globolus, Punica granatum, Bocconia arborea, Syzygium brazzavillense, Syzygium guineense, Carthamus tinctorius), Ginkgo biloba, Mosla chinensis, Salvia officinalis, and Cinnamomum cassia (extracts); Cryptolepis sanguinolenta (alkaloids, cryptolepine); Chelidonium majus (alkaloids, berberine, coptisine); Vitex agnus-castus (extract); Cladonia substellata (usnic acid); Fuligo septica, Tubifera microsperma (extract); Mundulea monantha, Tephrosia linearis (flavonoids); Lpomoea fistulosa (extract); Pimenta dioica (essential oils); Ratibida latipalearis, Teloxys graveolens, Dodonaea viscosa, Hypericum calycinum, Hyptis albida, Hyptis pectinata, Hyptis suaveolens and Hyptis verticillata (extracts); Asteriscus graveolones (bisabolone hydroperoxides); Derris scandens, Alnus rubra, Araliaceae family (extracts); Vinca rosea, Australian tea tree oil, peppermint oil, sage oil, thymol, eugenol and Thuja orientalis (extracts); Anacardium occidentale (phenolic lipids); Oidiodendron tenuissimum (extract); Acacia nilotica and Acacia farnesiana (polyphenol, tannin); Teminalia alata and Mallotus phillipinensis (extracts); Piectranthus grandidentatus (abientane diterpenoids); Pumica granatum and Datura metel (extracts); tea, Agave lecheguilla, Chamaesyce hirta, Baccharis glutinosa and Larrea tridentata (extracts); Camelia sinensis and Euphorbia hirta (theaflavin, polyphenon 60); Tabernaemontana pandacaqui, Yucca shidigera, Hemistepa lyrata, Yougia japonica, Prunella vulgaris, Lamium amplexicaule, Juniperus chinensis,

lxeris dentata, Gnaphalium affine, Chelidonium majus, Spirea prunifolia, Erythronium japonicum, Taxus wallichiana, Ganoderma lucidum Drava nemorosa, Youngia capillaris, Equisetum arvense, Australiam Lavender, Black Seed, Catuaba casca, Cineole, Damiana, Dicranum scoparium, Eucalptus oil, Ginger, and Grape seed (extracts); Neem seed, bark, and leaf extract; Neem oil; New Zealand Manuka extract; Nicotiana tabacum extract; olive leaf extract; a-pinene and b-pinene extracts; Rhubarb root extract; Syringa vulgaris extract; Tea tree oil (Terpinen-4-ol, a-terpinene, y-terpinene, a-terpineol, Terpinolene); Thyme (extract) and Vitamin E (extract).

WEST

Generate Collection

L1: Entry 7 of 12 File: EPAB Apr 29, 1999

PUB-NO: WO009921006A1
DOCUMENT-IDENTIFIER: WO 9921006 A1
TITLE: PHARMACEUTICAL GRADE VALERIAN, BLACK COHOSH, VITEX AGNUS-CASTUS, BILBERRY AND MILK THISTLE

PUBN-DATE: April 29, 1999

INVENTOR-INFORMATION:

NAME	COUNTRY
KHWAJA, TASNEEM A	US
FRIEDMAN, ELLIOT P	US

ASSIGNEE-INFORMATION:

NAME	COUNTRY
PHARMAPRINT INC	US
UNIV SOUTHERN CALIFORNIA	US
KHWAJA TASNEEM A	US
FRIEDMAN ELLIOT P	US

APPL-NO: US09822505
APPL-DATE: October 23, 1998

PRIORITY-DATA: US95541097A (October 23, 1997), US95661097A (October 23, 1997), US95541797A (October 23, 1997), US95661197A (October 23, 1997), US95661597A (October 23, 1997)

INT-CL (IPC): G01N 33/50; A61K 35/78
EUR-CL (EPC): A61K035/78

ABSTRACT:

The present invention relates generally to botanical valerian materials and methods for making such materials in medicinally useful and pharmaceutically acceptable forms. More particularly, the present invention relates to the use of compositional and bioactivity fingerprints in the processing of valerian, black cohosh, V. agnus-castus, bilberry or milk thistle materials to produce botanical products, such as drugs, which qualify as pharmaceutical grade compositions which are suitable for use in clinical or veterinary settings to treat and/or ameliorate diseases, disorders or conditions.

WEST

Generate Collection

L1: Entry 8 of 12 File: EPAB Aug 12, 1993

PUB-NO: DE003786425A1
DOCUMENT-IDENTIFIER: DE 3786425 A1
TITLE: TITLE DATA NOT AVAILABLE

PUBN-DATE: August 12, 1993

APPL-NO: DE03786425
APPL-DATE: May 2, 1987

PRIORITY-DATA: DE03786425A (May 2, 1987)

INT-CL (IPC): A61K 35/78

ABSTRACT:

Dopaminergic medicaments for treating diseases caused or influenced by dopamine deficiency contain an extract of Vitex agnus-castus. The extract is pref. an alcohol extract of Vitex fruits. The medicaments may be administered orally.

WEST

Generate Collection

L1: Entry 11 of 12 File: DWPI May 10, 1999

DERWENT-ACC-NO: 1999-302782
DERWENT-WEEK: 199938

TITLE: Preparation of pharmaceutical grade botanical material

INVENTOR: FRIEDMAN, E P; KHWAJA, T A

PATENT-ASSIGNEE:

ASSIGNEE	CODE
PHARMAPRINT INC	PHARN
UNIV SOUTH CAROLINA	UYSCN
UNIV SOUTHERN CALIFORNIA	UYSCN

PRIORITY-DATA: 1997US-0956615 (October 23, 1997), 1997US-0955410 (October 23, 1997), 1997US-0955417 (October 23, 1997), 1997US-0956610 (October 23, 1997), 1997US-0956611 (October 23, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 9913632 A	May 10, 1999		000	G01N033/50
WO 9921006 A1	April 29, 1999	E	138	G01N033/50

DESIGNATED-STATES: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
AU 9913632A	October 23, 1998	1999AU-0013632	
AU 9913632A		WO 9921006	Based on
WO 9921006A1	October 23, 1998	1998WO-US22505	

INT-CL (IPC): A61K 35/78; G01N 33/50

ABSTRACTED-PUB-NO: WO 9921006A
BASIC-ABSTRACT:

NOVELTY - A method for determining whether a botanical material is a pharmaceutical grade botanical product, comprising separating the botanical material to determine biological activity and comparing it to a standard, is new.

DETAILED DESCRIPTION - A method for determining whether a botanical material is a pharmaceutical grade botanical product, comprises:

(a) separating a representative aliquot of a botanical material having a given biological activity relevant to a specific condition, said botanical material selected from the group consisting of valerian, black cohosh, Vitex agnus castus,

bilberry, milk thistle, and a mixture of one of said botanicals and another plant material, comprising components, into marker fractions wherein at least one of the marker fractions comprises at least one active component;

(b) determining the degree of the given biological activity for each of the marker fractions in one or more bioassays relevant to the specific condition to provide a bioactivity fingerprint of the representative aliquot; and

(c) comparing the bioactivity fingerprint of the representative aliquot to a bioactivity fingerprint standard which has been established for a pharmaceutical grade botanical material to determine whether the material is pharmaceutical grade.

INDEPENDENT CLAIMS are also included for:

(1) a method for determining whether a botanical material is a pharmaceuti cal grade botanical product, comprising:

(a) providing a botanical material having a given biological activity relevant to a specific condition, said botanical material selected from the group consisting of valerian, black cohosh, vitex agnus-castus, bilberry, milk thistle, and a mixture of one of said botanicals and another plant material, which comprises components which have a given biological activity in one or more bioassays relevant to a specific condition and wherein each component has a standardized bioactivity profile;

(b) separating a representative aliquot from the material into marker fractions wherein at least one of the marker fractions comprises at least one of the active components;

(c) measuring the amount of each of the active components present in each of the marker fractions;

(d) calculating the bioactivity of each of the marker fractions based on the amount of each of the active components present and the standardized component bioactivity profile to provide a calculated bioactivity fingerprint of the representative aliquot; and

(e) comparing the calculated bioactivity fingerprint of the representative aliquot to a bioactivity fingerprint standard which has been established for a pharmaceutical grade botanical to determine whether the material is pharmaceutical grade;

(2) a method for determining whether a botanical material is a pharmaceuti cal grade botanical product comprises determining a total bioactivity of a representative aliquot of a valerian material using a GABAA assay and a dopamine uptake assay and comparing the total bioactivity of the representative aliquot with that of a standard to determine whether the valerian material is a pharmaceutical grade valerian;

(3) a method for making pharmaceutical grade black cohosh which comprises determining a total bioactivity of a representative aliquot of a black cohosh material using an estradiol binding assay and an oxytocin receptor binding assay and comparing the total bioactivity of the representative aliquot with that of a standard to determine whether the black cohosh material is a pharmaceutical grade black cohosh;

(4) a method for determining V. agnus-castus of pharmaceutical grade, comprising determining a total bioactivity of e representative aliquot of V. agnus-castus material using a dopamine D2 agonist assay and a glucocorticoid receptor assay and comparing the total bioactivity of the representative aliquot with that of a standard to determine whether the V. agnus-castus material is a pharmaceutical grade V. agnus-castus;

(5) a method for determining whether bilberry or milk thistle is pharmaceutical

grade bilberry or milk thistle which comprises determining a total bioactivity of a representative aliquot using a PAF-R assay and comparing the total bioactivity of the representative aliquot with that of a standard to determine whether the bilberry or milk thistle material is a pharmaceutical grade bilberry or milk thistle;

(6) pharmaceutical grade botanical as determined by any of the methods above.

USE - The pharmaceutical grade valerian or a mixture of valerian and another plant material is used for treating or ameliorating a nervous system disorder or a sleep or psychological disorder.

Pharmaceutical grade black cohosh or a mixture of black cohosh and another plant material, comprising flavonoids, glycosides, steroids and terpenoids, especially actein or formonentin, is used for treating or ameliorating a gynecological disorder.

Pharmaceutical grade V. agnus-castus or a mixture of V. agnus-castus and another plant material is used for treating or ameliorating a menstrual disorder.

Pharmaceutical grade bilberry or a mixture of bilberry and another plant, comprising anthocyanidins, carbohydrates, carotenoids, fatty acids, flavonoids, isoprenoids, phenolics, polyketides, prostaglandins and terpenoids, is used for treating or ameliorating a disorder or disease selected from an inflammatory disorder, a cardiovascular disorder, a gastrointestinal disorder, a metabolic disorder and an ophthalmologic disorder.

Pharmaceutical grade milk thistle or a mixture of milk thistle and another plant, comprising carbohydrates, fatty acids, fatty acid esters, flavanolignans, peptides, phenolics and terpenoids, is used for treating or ameliorating a disorder or disease selected from the group consisting of: an allergic disorder, an inflammatory disorder, a cardiovascular disorder, a gastrointestinal disorder, a metabolic disorder, a disease induced by a microbial organism (all claimed).

ADVANTAGE - The process ensures that only botanical material of a constant quality is used for the treatment of above conditions. It provides the means of isolating the essentially active parts of the plant, while discarding non-essential parts of the plant.

TITLE-TERMS: PREPARATION PHARMACEUTICAL GRADE BOTANICAL MATERIAL

DERWENT-CLASS: B04 C03 D16 S03

CPI-CODES: B04-A10; B14-A01; B14-C03; B14-D01; B14-E10B; B14-F01; B14-G02A; B14-N03; C04-A10; C14-A01; C14-C03; C14-D01; C14-E10B; C14-F01; C14-G02A; C14-N03; D05-H09;

EPI-CODES: S03-E14H;

CHEMICAL-CODES:

Chemical Indexing M1 *01*
Fragmentation Code
M423 M720 M905 N161 P001 P200 P210 P220 P241 P420
P431 P520 P522 P625 P714 P922 Q233
Specfic Compounds
A00GTK A00GTT A00GTP

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C1999-088838
Non-CPI Secondary Accession Numbers: N1999-226819

WEST

End of Result Set

☐ Generate Collection Print

L8: Entry 62 of 62 File: DWPI Feb 26, 1981

DERWENT-ACC-NO: 1981-28298D
DERWENT-WEEK: 198116

TITLE: Antiinflammatory obtd. from Eucalyptus plants - by extn. with solvent e.g. n-hexane

PATENT-ASSIGNEE:

ASSIGNEE	CODE
TAKEDA CHEM IND LTD	TAKE

PRIORITY-DATA: 1979JP-0097782 (July 30, 1979)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 56020597 A	February 26, 1981		000	

INT-CL (IPC): A61K 35/78; C07G 17/00

ABSTRACTED-PUB-NO: JP 56020597A
BASIC-ABSTRACT:

Extract EK of Eucalyptus plants is new having antiinflammatory activity, which does not distil by steam distn. and shows an Rf value of Ca 0.4 in TLC using a silica gel plate and non-hexane-ethyl acetate (20:1 by vol.) as a developing solvent.

Extract is prepd. by extracting plants of the genus Eucalyptus with a solvent (e.g. n-hexane, cyclohexane, ethyl ether, acetone or dichloromethane) and recovering EK from the extract.

TITLE-TERMS: ANTIINFLAMMATORY OBTAIN EUCALYPTUS PLANT EXTRACT SOLVENT N HEXANE

DERWENT-CLASS: B04

CPI-CODES: B04-A07F; B12-D07;

CHEMICAL-CODES:

Chemical Indexing M1 *01*
Fragmentation Code
V400 V406 P420 M710 M423 M902

WEST

Generate Collection Print

L6: Entry 147 of 162 File: DWPI Nov 10, 1998

DERWENT-ACC-NO: 1999-040626
DERWENT-WEEK: 200002

TITLE: Cell adhesion inhibitor used for cancer metastasis inhibitor, etc. - contains effective ingredients of Apocynaceae family, Cebera manghas L., Moraceae family, Ficus septica and/or Smilacaceae family, Hedyotis verticitlata plants or their extracts

PATENT-ASSIGNEE:

ASSIGNEE	CODE
ASAHI KASEI KOGYO KK	ASAH

PRIORITY-DATA: 1997JP-0127859 (May 2, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 10298089 A	November 10, 1998		004	A61K035/78

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
JP 10298089A	May 2, 1997	1997JP-0127859	

INT-CL (IPC): A61 K 35/78

ABSTRACTED-PUB-NO: JP 10298089A
BASIC-ABSTRACT:

Cell adhesion inhibitor contains effective ingredients of Apocynaceae family, Cebera manghas L., Moraceae family, Ficus septica and/or Smilacaceae family, Hedyotis verticitlata plants or their extracts.

Whole or parts of plants or their extracts with water and/or organic solvents e.g. petroleum ether, hydrocarbons, halohydrocarbons, alcohols and pyridine are preferably used or processed by conventional purification.

USE - The inhibitor is used for antiallergic agent, immunosuppressor or cancer metastasis inhibitor. The dosage is 0.01-10 mg/kg/day orally, intestinally or externally.

ADVANTAGE - The inhibitor inhibits expression of cell adhesion molecules of vascular endothelial cells with low toxicity.

CHOSEN-DRAWING: Dwg.0/0

TITLE-TERMS: CELL ADHESIVE INHIBIT CANCER METASTASIS INHIBIT CONTAIN EFFECT INGREDIENT FAMILY FAMILY FAMILY PLANT EXTRACT

DERWENT-CLASS: B04

WEST

Freeform Search

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Term: chaste lamb

Display: 10 **Documents in Display Format:** CIT **Starting with Number** 20

Generate: ○ Hit List ◉ Hit Count ○ Image

Search | Clear | Help | Logout | Interrupt

Main Menu | Show S Numbers | Edit S Numbers | Preferences

Search History

Today's Date: 1/2/2002

DB Name	Query	Hit Count	Set Name
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	chaste lamb	1	L2
USPT,PGPB,JPAB,EPAB,DWPI,TDBD	agnus-castus	12	L1

```
=> d his

     (FILE 'HOME' ENTERED AT 12:48:50 ON 02 JAN 2002)

     FILE 'CA, BIOSIS, MEDLINE' ENTERED AT 12:51:04 ON 02 JAN 2002
L1           165 S AGNUS-CASTUS?
L2           127 DUP REM L1 (38 DUPLICATES REMOVED)
L3          8973 S COX-2
L4             0 S L2 AND L3
L5        541103 S INFLAMM?
L6          4183 S L5 AND L3
L7        767306 S EXTRACT?
L8           153 S L7 (P) L3
L9            64 S L6 AND L8
L10           45 DUP REM L9 (19 DUPLICATES REMOVED)
L11         8973 S COX-2
L12           45 S L11 AND L10
L13        30912 S ORGANIC SOLVENT?
L14            0 S L12 AND L13

=>
```

```
Trying 3106016892...Open

Welcome to STN International!  Enter x:x
LOGINID:ssspta1815mxw
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Dec 17  The CA Lexicon available in the CAPLUS and CA files
 NEWS  3  Feb 06  Engineering Information Encompass files have new names
 NEWS  4  Feb 16  TOXLINE no longer being updated
 NEWS  5  Apr 23  Search Derwent WPINDEX by chemical structure
 NEWS  6  Apr 23  PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
 NEWS  7  May 07  DGENE Reload
 NEWS  8  Jun 20  Published patent applications (A1) are now in USPATFULL
 NEWS  9  JUL 13  New SDI alert frequency now available in Derwent's
                  DWPI and DPCI
 NEWS 10  Aug 23  In-process records and more frequent updates now in
                  MEDLINE
 NEWS 11  Aug 23  PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
 NEWS 12  Aug 23  Adis Newsletters (ADISNEWS) now available on STN
 NEWS 13  Sep 17  IMSworld Pharmaceutical Company Directory name change
                  to PHARMASEARCH
 NEWS 14  Oct 09  Korean abstracts now included in Derwent World Patents
                  Index
 NEWS 15  Oct 09  Number of Derwent World Patents Index updates increased
 NEWS 16  Oct 15  Calculated properties now in the REGISTRY/ZREGISTRY File
 NEWS 17  Oct 22  Over 1 million reactions added to CASREACT
 NEWS 18  Oct 22  DGENE GETSIM has been improved
 NEWS 19  Oct 29  AAASD no longer available
 NEWS 20  Nov 19  New Search Capabilities  USPATFULL and USPAT2
 NEWS 21  Nov 19  TOXCENTER(SM) - new toxicology file now available on STN
 NEWS 22  Nov 29  COPPERLIT now available on STN
 NEWS 23  Nov 29  DWPI revisions to NTIS and US Provisional Numbers
 NEWS 24  Nov 30  Files VETU and VETB to have open access
 NEWS 25  Dec 10  WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
 NEWS 26  Dec 10  DGENE BLAST Homology Search
 NEWS 27  Dec 17  WELDASEARCH now available on STN
 NEWS 28  Dec 17  STANDARDS now available on STN
 NEWS 29  Dec 17  New fields for DPCI
 NEWS 30  Dec 19  CAS Roles modified
 NEWS 31  Dec 19  1907-1946 data and page images added to CA and CAplus

 NEWS EXPRESS  August 15 CURRENT WINDOWS VERSION IS V6.0c,
               CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP),
               AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
```

research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:48:50 ON 02 JAN 2002

=> file ca, biosis, medline

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.60	0.60

FILE 'CA' ENTERED AT 12:51:04 ON 02 JAN 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 12:51:04 ON 02 JAN 2002
COPYRIGHT (C) 2002 BIOSIS(R)

FILE 'MEDLINE' ENTERED AT 12:51:04 ON 02 JAN 2002

=> s agnus-castus?
L1 165 AGNUS-CASTUS?

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2 127 DUP REM L1 (38 DUPLICATES REMOVED)

=> s cox-2
L3 8973 COX-2

=> s l2 and l3
L4 0 L2 AND L3

=> s inflamm?
L5 541103 INFLAMM?

=> s l5 and l3
L6 4183 L5 AND L3

=> s extract?
L7 767306 EXTRACT?

=> s l7 (p) l3
L8 153 L7 (P) L3

=> s l6 and l8
L9 64 L6 AND L8

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10 45 DUP REM L9 (19 DUPLICATES REMOVED)

=> cox-2
COX-2 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

```
=> s cox-2
L11       8973 COX-2

=> s l11 and l10
L12         45 L11 AND L10

=> s organic solvent?
L13      30912 ORGANIC SOLVENT?

=> s l12 and l13
L14          0 L12 AND L13

=> d l12 1-45 ab,bib

L12  ANSWER 1 OF 45  BIOSIS  COPYRIGHT 2002 BIOSIS
AB   Objective and design: CD44 is the major cell surface receptor for
     hyaluronan (HA) on macrophages. Stimulation of macrophages via the
HA-CD44
     pathway leads to the enhanced expression of inflammatory gene
     products, including cytokines, chemokines, and adhesion molecules. We
have
     examined whether activation of CD44 by crosslinking is capable of
     activating the cyclooxygenase (COX) and prostaglandin (PG)/thromboxane
     (TX) pathway in cultured macrophages. Materials and methods: CD44 was
     crosslinked on RAW 264.7 mouse macrophages using specific rat anti-mouse
     CD44 monoclonal antibodies and anti-rat IgG. Total RNA was
     extracted and subjected to RT-PCR analysis for genes of the PG/TX
     synthetic pathway. Supernatants were analyzed for PGE2 and TXB2 using
     specific ELISAs. Results: Transcripts for COX-1, COX-2
     , TX synthase (TXS), and PGE2 synthase (PGES) were all constitutively
     expressed in the mouse macrophage cell line RAW 264.7. Crosslinking of
     CD44 markedly enhanced COX-2 and weakly increased TXS
     mRNA, whereas COX-1 and PGES mRNA did not change significantly in these
     cells. Crosslinking of CD44 selectively increased the production of TXB2
     but not PGE2. Conclusions: These findings suggest that the activation of
     the CD44 pathway plays a unique role in PG synthesis. Activation of this
     pathway results in enhanced TXA2 but not PGE2 production. This leads to
an
     imbalance of the TXA2/PGE2 profile which favors a proinflammatory and
     vasoconstrictory response.
AN   2002:10274  BIOSIS
DN   PREV200200010274
TI   CD44-mediated cyclooxygenase-2 expression and thromboxane A2 production
in
     RAW 264.7 macrophages.
AU   Sun, L. K.; Wahl, P.; Bilic, G.; Wuthrich, R. P. (1)
CS   (1) Division of Nephrology, Department of Medicine, Kantonsspital,
     Rorschacherstrasse 95, CH-9007, Saint Gallen: rpw@kssg.ch Switzerland
SO   Inflammation Research, (October, 2001) Vol. 50, No. 10, pp. 496-499.
     print.
     ISSN: 1023-3830.
DT   Article
LA   English

L12  ANSWER 2 OF 45  BIOSIS  COPYRIGHT 2002 BIOSIS
AB   Large amounts of anti-inflammatory activity are present in
```

extracts prepared from Eucomis plants. **Extracts** prepared from in vitro plantlets grown on a modified Murashige and Skoog medium supplemented with 1 mg l-1 NAA and 1 mg l-1 BA, were tested in two cyclooxygenase assays (COX-1 and **COX-2**). Ethanol **extracts** showed high levels of COX-1 and **COX-2** inhibitory activity, with a **COX-2**/COX-1 inhibition ratio of 1.1. Further experimental work aimed to determine the factors affecting the accumulation of anti-**inflammatory** compounds in in vitro plantlets. High concentrations of sucrose (40 g l-1) in the culture medium significantly increased the number of shoots initiated, but had no effect on the subsequent anti-**inflammatory** activity. Low concentrations of sucrose (10 g l-1) led to a significant decrease in COX-1 inhibition. Changig the amount of nitrogen in the medium (but not the ratio of nitrate to ammonium ions) had no significant effect on the COX-1 inhibitory activity of the **extracts**.

AN 2001:569239 BIOSIS
DN PREV200100569239
TI The effect of nitrogen and sucrose concentrations on the growth of Eucomis autumnalis (Mill.) Chitt. plantlets in vitro, and on subsequent anti-**inflammatory** activity in extracts prepared from the plantlets.
AU Taylor, J. L. S.; van Staden, J. (1)
CS (1) Research Centre for Plant Growth and Development, School of Botany and Zoology, University of Natal Pietermaritzburg, Scottsville, 3209 South Africa
SO Plant Growth Regulation, (May, 2001) Vol. 34, No. 1, pp. 49-56. print. ISSN: 0167-6903.
DT Article
LA English
SL English

L12 ANSWER 3 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB To further examine the organ-specific toxic effects of selective and non-selective **COX-2** inhibitors in adjuvant arthritis (CAA), we assessed the PGE2 concentration in various organs. AA was induced by intradermal injection of Mycobacterium butyricum. Fourteen days after inoculation, AA rats were selected and treated orally every day for two weeks with the selective **COX-2** inhibitor, flosulide, or the COX-1-**COX-2** inhibitor, indomethacin. The time-course of paw swelling was determined. At the end of treatments, PGE2 was **extracted** from paw, stomach (wall and mucosa) and kidney and its concentration was determined by ELISA. Paw edema increase was accompanied by a rise in PGE2 concentration. PGE2 also increased in stomach (mucosa and wall) and kidney. The anti-**inflammatory** treatment with flosulide (5 mg/kg X day), and indomethacin (1 mg/kg X day), reduced plantar edema by 98.0% and 74.4% respectively. Both drugs greatly decreased PGE2 levels in paw (73.7-53.2%), stomach wall (84.5-80.3%), stomach mucosa (109.9-110.9%) and kidney (92.9-97.5% respectively). However, PGE2 reductions in AA rats did not fall significantly below control values.
AN 2001:442030 BIOSIS
DN PREV200100442030
TI Changes in prostaglandin E2 (PGE2) levels in paw exudate, stomach and kidney of arthritic rats: Effects of flosulide.
AU Turull, Angels; Queralt, Josep (1)
CS (1) Departament de Fisiologia, Divisio IV, Facultat de Farmacia, Universitat de Barcelona, Barcelona: jregue@farmacia.far.ub.es Spain
SO Prostaglandins & Other Lipid Mediators, (August, 2001) Vol. 66, No. 1, pp.

27-37. print.
ISSN: 1098-8823.
DT Article
LA English
SL English

L12 ANSWER 4 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB An herbal composition reducing **inflammation** in bones and joints by inhibiting the enzyme cyclooxygenase-2 is prepared from holy basil, turmeric, ginger, green tea, rosemary, huzhang, Chinese goldthread, barberry, oregano and scutellariae baicalensis. More particularly, the herbal composition of the present invention contains therapeutically effective amounts of the supercritical **extracts** of ginger, rosemary and oregano, and therapeutically effective amounts of **extracts** of holy basil, turmeric, green tea, huzhang, Chinese goldthread, barberry, rosemary and scutellariae baicalensis. The herbal composition can be administered orally, topically or parenterally. Particularly preferred embodiments are soft gel capsules for oral administration and creams for topical application. In addition to reducing **inflammation**, the herbal composition also promotes healthy joint function and, because it inhibits cyclooxygenase-2 (**COX-2**), the composition also promotes normal cell growth. Furthermore, the herbal composition contains organic anti-aging constituents that inactivate oxygen free radicals, thereby providing antioxidant benefits in addition to anti-**inflammatory** benefits.
AN 2001:436170 BIOSIS
DN PREV200100436170
TI Herbal composition for reducing **inflammation** and methods of using same.
AU Newmark, Thomas; Schulick, Paul
PI US 6264995 July 24, 2001
SO Official Gazette of the United States Patent and Trademark Office Patents, (July 24, 2001) Vol. 1248, No. 4, pp. No Pagination. e-file.
ISSN: 0098-1133.
DT Patent
LA English

L12 ANSWER 5 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Various **extracts** prepared from the traditional dye and medicinal plant Isatis tinctoria L. were submitted to a broad in vitro screening against 16 anti-**inflammatory** targets. Dichloromethane (DCM) **extracts** from dried leaves showed a marked cyclooxygenase (COX) inhibitory activity with a preferential effect on **COX-2** catalysed prostaglandin synthesis. A supercritical fluid **extraction** (SFE) procedure employing CO2-modifier mixtures was developed by which the bioactivity profile and chromatographic fingerprint of the DCM **extract** could be reproduced. High-resolution activity directed on-line identification of the **COX-2** inhibitory principle, using a combination of LC-DAD-MS with a microtitre-based bioassay, led to the identification of tryptanthrin (1) as the constituent responsible for essentially all **COX-2** inhibitory activity in the crude **extract**. Following on-line identification, 1 was isolated at preparative scale and its structure confirmed by comparison with synthetic tryptanthrin. In an assay with lipopolysaccharide stimulated Mono Mac 6 cells, tryptanthrin (1) was of comparable potency (IC50 = 64 nM) than the preferential **COX-**

2 inhibitors nimesulide (IC50 = 39 nM) and NS 398 (IC50 = 2 nM). The SFE **extract** and 1 showed no cytotoxicity in Mono Mac 6 and RAW 264.7 cells when tested at 100 mug/ml and 10 muM, respectively.

AN 2001:408585 BIOSIS
DN PREV200100408585
TI Identification and isolation of the cyclooxygenase-2 inhibitory principle in Isatis tinctoria.
AU Danz, Henning; Stoyanova, Stefka; Wippich, Petra; Brattstroem, Axel; Hamburger, Matthias (1)
CS (1) Institut fuer Pharmazie, Friedrich-Schiller-Universitaet Jena, Semmelweisstrasse 10, 07743, Jena: B7HAMA@rz.uni-jena.de Germany
SO Planta Medica, (July, 2001) Vol. 67, No. 5, pp. 411-416. print. ISSN: 0032-0943.
DT Article
LA English
SL English

L12 ANSWER 6 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB 1 We investigated the mechanism of suppression of inducible nitric oxide synthase (iNOS) and cyclo-oxygenase-2 (**COX-2**) by ergolide, sesquiterpene lactone from Inula britannica. 2 iNOS activity in cell-free **extract** of LPS/IFN-gamma-stimulated RAW 264.7 macrophages was markedly attenuated by the treatment with ergolide. Its inhibitory effect on iNOS was paralleled by decrease in nitrite accumulation in culture medium of LPS/IFN-gamma-stimulated RAW 264.7 macrophages in a concentration-dependent manner. However, its inhibitory effect does not result from direct inhibition of the catalytic activity of NOS. 3 Ergolide markedly decreased the production of prostaglandin E2 (PGE2) in cell-free **extract** of LPS/IFN-gamma-stimulated RAW 264.7 macrophages in a concentration-dependent manner, without alteration of the catalytic activity of **COX-2** itself. 4 Ergolide decreased the level of iNOS and **COX-2** protein, and iNOS mRNA caused by stimulation of LPS/IFN-gamma in a concentration-dependent manner, as measured by Western blot and Northern blot analysis, respectively. 5 Ergolide inhibited nuclear factor-kappaB (NF-kappaB) activation, a transcription factor necessary for iNOS and **COX-2** expression in response to LPS/IFN-gamma. This effect was accompanied by the parallel reduction of nuclear translocation of subunit p65 of NF-kappaB as well as IkappaB-alpha degradation. In addition, these effects were completely blocked by treatment of cysteine, indicating that this inhibitory effect of ergolide could be mediated by alkylation of NF-kappaB itself or an upstream molecule of NF-kappaB. 6 Ergolide also directly inhibited the DNA-binding activity of active NF-kappaB in LPS/IFN-gamma-pretreated RAW 264.7 macrophages. 7 These results demonstrate that the suppression of NF-kappaB activation by ergolide might be attributed to the inhibition of nuclear translocation of NF-kappaB resulted from blockade of the degradation of IkappaB and the direct modification of active NF-kappaB, leading to the suppression of the expression of iNOS and **COX-2**, which play important roles in **inflammatory** signalling pathway.
AN 2001:367265 BIOSIS
DN PREV200100367265
TI Ergolide, sesquiterpene lactone from Inula britannica, inhibits inducible nitric oxide synthase and cyclo-oxygenase-2 expression in RAW 264.7 macrophages through the inactivation of NF-kappaB.
AU Han, Jeung Whan; Lee, Byeong Gon; Kim, Yong Kee; Yoon, Jong Woo; Jin, Hye Kyoung; Hong, Sungyoul; Lee, Hoi Young; Lee, Kang Ro; Lee, Hyang Woo (1)
CS (1) College of Pharmacy, Sungkyunkwan University, Suwon, 440-746:

hylee@yurim.skku.ac.kr South Korea
SO British Journal of Pharmacology, (June, 2001) Vol. 133, No. 4, pp. 503-512. print.
ISSN: 0007-1188.
DT Article
LA English
SL English

L12 ANSWER 7 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Chronic ethanol feeding at a constant rate results in cyclic peaks (P) and troughs (T) in urinary alcohol levels (UALs). Recently we have shown (Li et al. Am J. Physiol Gastrointest Liver Physiol, 2000) that the UAL cycle may be regulated by the intact hypothalamic-pituitary thyroid axis. In the present study the expression of oxidative, apoptotic and **inflammatory** genes was investigated by RT-PCR in rat livers at P and T UALs in order to compare the mechanism of liver injury at these two phases of the UAL cycle. Male Wistar rats were either fed ethanol (13 g/kg/day, n=10) or isocaloric dextrose (n=5) for one month and killed at P or T UAL. The liver was frozen in liquid N2. Total RNA was **extracted** by the Trizol method and RT-PCR was done by standard methods using gene specific primers. Band density was normalized by either 18S rRNA or GAPDH. Liver/body wt. ratio and pathology score differed significantly between the control and P and T UAL groups. Expression of VEGF, CYP2E1 and CTGF were significantly higher at P and T than controls. Expression of hypoxia response genes EPO, but not HIF-1a or HO-1, was higher at the P compared to the T and controls. Expression of iNOS, **COX-2**, HSP70, proteasome 26S, and MCP-1 but not TNF-a, differed significantly at P and T. Bax, but not Fas/FasL expression was upregulated at the T compared to the P and controls. MnSOD but not Cu-ZnSOD expression was higher at the T compared to P and controls ($P<0.05$). For the first time, a significant difference in hypoxia response, oxidative stress, proinflammatory and apoptotic genes between P and T was shown. Interestingly, genes associated exclusively with mitochondria (iNOS, Bax and MnSOD) differed significantly between P and T. Genes associated with hypoxia were upregulated at P.Genes associated with oxidative stress were upregulated at P and T. Apoptotic gene Bax was upregulated T. These results suggest that the mechanism of ethanol injury is different at the P and T: ie hypoxia induced oxidative stress at P and apoptosis at T.
AN 2001:292964 BIOSIS
DN PREV200100292964
TI Effect of ethanol cycling on gene expression in intragastric ethanol feeding rat model of alcoholic liver disease.
AU Shahed, Asha R. (1); Li, Jun (1); Yuan, Q. I. (1); French, Samuel William (1)
CS (1) Harbor-UCLA Med. Center, 1000 Carson St W, Torrance, CA, 90509 USA
SO FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A609. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638.
DT Conference
LA English
SL English

L12 ANSWER 8 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Cyclooxygenase-2 (**COX-2**) is a recognized target for cancer prevention and possibly treatment. To identify novel inhibitors of **COX-2**, we developed a high throughput reporter gene assay that utilizes a region of the human **COX-2** promoter to drive luciferase expression. A total of 968 **extracts** from 266 plants were screened. **Extracts** from 12 plants (4.5%), including Arnebia euchroma, a medicinal plant used in the Far East to treat **inflammation**, inhibited the stimulation of **COX-2** promoter activity. The gene promoter assay then was used to identify shikonin, a compound with known anti-**inflammatory** and chemopreventive properties, as an active compound in A. euchroma. To complement the gene promoter studies, we determined the effects of a mixture of shikonins on phorbol 12-myristate 13-acetate (PMA)-mediated induction of **COX-2** in transformed human mammary epithelial cells. Shikonins inhibited PMA-mediated induction of **COX-2** mRNA, protein, and prostaglandin E2 synthesis. In transient transfections, PMA caused a severalfold increase in **COX-2** promoter activity, an effect that was suppressed by shikonins. Shikonins also inhibited PMA-mediated stimulation of extracellular signal-regulated kinase1/2 mitogen-activated protein kinases and activator protein-1 activity. Collectively, these results demonstrate the successful development and use of a high throughput reporter gene assay for the identification of a novel inhibitor of **COX-2** expression.
AN 2001:283657 BIOSIS
DN PREV200100283657
TI Development and use of a gene promoter-based screen to identify novel inhibitors of cyclooxygenase-2 transcription.
AU Subbaramaiah, Kotha; Bulic, Predrag; Lin, Yuan; Dannenberg, Andrew J.; Pasco, David S. (1)
CS (1) National Center for Natural Products Research, University of Mississippi, University, MS, 38677: dpasco@olemiss.edu USA
SO Journal of Biomolecular Screening, (April, 2001) Vol. 6, No. 2, pp. 101-110. print.
ISSN: 1087-0571.
DT Article
LA English
SL English

L12 ANSWER 9 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB We determined the effects of a crude green tea **extract** given as drinking fluid on the promotion/progression phase of colon carcinogenesis in rats after induction of the neoplastic process by azoxymethane. Adult Wistar rats were given azoxymethane (15 mg/kg ip) once a week for two weeks. One week after the second injection, the rats were randomly divided into two groups. One group (n = 8) received daily prepared aqueous solutions of green tea **extracts** (GTE; 0.02%, wt/vol); the control group (n = 8) received tap water. After six weeks, rats receiving GTE showed a 60% reduction in the number of colonic preneoplastic lesions (aberrant crypts). The number of individual crypts per aberrant crypt focus (crypt multiplicity) was significantly reduced in the GTE group; the majority (80%) of the remaining aberrant foci contained only one or two preneoplastic crypts. A significant and selective decrease of cyclooxygenase (**COX**)-2 activity was observed in the colon of rats receiving GTE (23 +- 3 vs. 117 +- 30 mU/mg protein in controls), whereas COX-1 showed no alterations. Our data demonstrate that

GTE reduces **COX-2** and suppresses the formation of colonic preneoplastic lesions. They provide new insights into the mechanism of chemopreventive and anti-**inflammatory** properties of green tea.

AN 2001:262900 BIOSIS
DN PREV200100262900
TI Suppression of azoxymethane-induced preneoplastic lesions and inhibition of cyclooxygenase-2 activity in the colonic mucosa of rats drinking a crude green tea extract.
AU Metz, Nadia; Lobstein, Annelise; Schneider, Yann (1); Gosse, Francine (1); Schleiffer, Rene (1); Anton, Robert; Raul, Francis (1)
CS (1) Laboratoire du Controle Metabolique et Nutritionnel en Oncologie Digestive, Universite Louis Pasteur, Institut de Recherche Contre les Cancers de l'Appareil Digestif, 67091, Strasbourg-Cedex France
SO Nutrition and Cancer, (2000) Vol. 38, No. 1, pp. 60-64. print. ISSN: 0163-5581.
DT Article
LA English
SL English

L12 ANSWER 10 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB 1 The effect of two derivatives of salicylate, 2-hydroxy-4-trifluoromethylbenzoic acid (HTB) and 2-acetoxy-4-trifluoromethylbenzoic acid (triflusal), on the expression of several proteins displaying proinflammatory activities the regulation of which is associated to the transcription factor NF-kappaB, was assayed in the human astrocytoma cell line 1321N1. 2 Tumour necrosis factor-alpha (TNF-alpha) activated NF-kappaB as judged from both the appearance of kappaB-binding activity in the nuclear **extracts**, the degradation of IkappaB proteins in the cell lysates, and the activation of IkappaB kinases using an immunocomplex kinase assay with glutathione S-transferase (GST)-IkappaB proteins as substrates. 3 HTB up to 3 mM did not inhibit the nuclear translocation of NK-kappaB/Rel proteins as judged from electrophoretic mobility-shift assays; however, HTB inhibited the degradation of IkappaBbeta without significantly affecting the degradation of both IkappaBalpha and IkappaBepsilon. 4 In keeping with their inhibitory effect on IkappaBbeta degradation in the cell lysates, both HTB and triflusal inhibited the phosphorylation of GST-IkappaBbeta elicited by TNF-alpha, without affecting the phosphorylation of GST-IkappaBalpha. 5 The effect of both HTB and triflusal on kappaB-dependent trans-activation was studied by assaying the expression of both cyclo-oxygenase-2 (**COX-2**) and vascular cell adhesion molecule-1 (VCAM-1). HTB and triflusal inhibited in a dose-dependent manner the expression of **COX-2** and VCAM-1 mRNA and the induction of **COX-2** protein at therapeutically relevant concentrations. 6 These findings show the complexity of the biochemical mechanisms underlying the activation of NF-kappaB in the different cell types and extend the anti-**inflammatory** effects of HTB and triflusal to neural cells.
AN 2001:161402 BIOSIS
DN PREV200100161402
TI Effect of 4-trifluoromethyl derivatives of salicylate on nuclear factor kappaB-dependent transcription in human astrocytoma cells.
AU Hernandez, Marita; Fernandez de Arriba, Alberto; Merlos, Manel; Fuentes, Lucia; Sanchez Crespo, Mariano (1); Nieto, Maria Luisa
CS (1) Instituto de Biologia y Genetica Molecular, Facultad de Medicina, 47005, Valladolid: mscres@ibgm.uva.es Spain
SO British Journal of Pharmacology, (January, 2001) Vol. 132, No. 2, pp.

547-555. print.
ISSN: 0007-1188.
DT Article
LA English
SL English

L12 ANSWER 11 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB 1 The effect of endogenous glucocorticoid hormones on the expression of rat B1 receptors was examined by means of molecular and pharmacological functional approaches. 2 Rats were adrenalectomized (ADX), and 7 days after this procedure the intradermal injection of B1 receptor agonist des-Arg9-BK produced a significant increase in the paw volume, while only a weak effect was observed in sham-operated animals. A similar increase in the contractile responses mediated by B1 agonist des-Arg9-BK was also observed in the rat portal vein in vitro. 3 Chemical ADX performed with mitotane (a drug that reduces corticosteroid synthesis) produced essentially the same up-regulation of B1 receptors as that observed in ADX rats. 4 The modulation of B1 receptor expression was evaluated by ribonuclease protection assay, employing mRNA obtained from the lungs and paw of ADX rats. 5 Additionally, both paw oedema and contraction of portal vein mediated by B1 agonist des-Arg9-BK in ADX rats, were markedly inhibited by treatment with dexamethasone, or **COX-2** inhibitor meloxican, or with the NF-kappaB inhibitor PDTC. Interestingly, the same degree of inhibition was achieved when the animals were treated with a combination of submaximal doses of dexamethasone and PDTC. 6 The involvement of NF-kappaB pathway was further confirmed by mobility shift assay using nuclear **extracts** from lung, paw and heart of ADX rats. It was also confirmed that the treatment of ADX rats with dexamethasone, PDTC or dexamethasone plus PDTC completely inhibit NF-kappaB activation caused by absence of endogenous glucucorticoid. 7 Together, the results of the present study provide, for the first time, molecular and pharmacological evidence showing that B1 kinin receptor expression can be regulated through endogenous glucocorticoids by a mechanism dependent on NF-kappaB pathway. Clinical significance of the present findings stem from evidence showing the importance of B1 kinin receptors in the mediation of **inflammatory** and pain related responses.
AN 2001:150704 BIOSIS
DN PREV200100150704
TI Molecular and pharmacological evidence for modulation of kinin B1 receptor expression by endogenous glucocorticoids hormones in rats.
AU Cabrini, Daniela A.; Campos, Maria M.; Tratsk, Karla S.; Merino, Vanessa F.; Silva, Jose A., Jr.; Souza, Gloria E. P.; Avellar, Maria C. W.; Pesquero, Joao B.; Calixto, Joao B. (1)
CS (1) Departamento de Farmacologia, Universidade Federal de Santa Catarina, Rua Ferreira Lima, 82, 88015-420, Florianopolis, SC: calixto@farmaco.ufsc.br Brazil
SO British Journal of Pharmacology, (January, 2001) Vol. 132, No. 2, pp. 567-577. print.
ISSN: 0007-1188.
DT Article
LA English
SL English

L12 ANSWER 12 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Prostanoids formed by cyclooxygenase (COX) play an important role in the

induction of pain and **inflammation**. While both isoforms of COX are inducible under certain circumstances, it is generally believed that COX-1 is constitutively expressed while **COX-2** is inducible during **inflammation**. Celecoxib (Celebrex) is a COX inhibitor which has been shown in in vitro and ex vivo studies to be highly selective for **COX-2**. We conducted a double-blind, randomized, placebo and active comparator controlled clinical trial to determine whether estimates of selectivity based on in vitro and ex vivo analyses are reliable indicators of in vivo selectivity.

Subjects, N=60 outpatients undergoing the surgical removal of two impacted mandibular third molars, received either celecoxib (200 mg), ibuprofen (600 mg) or a matching placebo tablet 8 hours prior to surgery and a second dose 1 hour before surgery. At the conclusion of surgery, microdialysis (20 kd MW cutoff) probes were placed into the **extraction** sites for collection of samples for the measurement of prostaglandin E2 (a product of both COX-1 & **COX-2**) and thromboxane B2 (a product of COX-1). Vials for sample collection were changed every 20 minutes and pain intensity was estimated concurrently with a visual analog scale for 4 hours postoperatively. Results demonstrated a significant analgesic effect (repeated measures ANOVA, $P<0.01$) with celecoxib being intermediate between ibuprofen and placebo. A similar relationship was seen for the suppression of PGE2 at time points consistent with COX-1 activity (repeated measures ANOVA, $P<0.01$). The suppression of products of COX-1 with pain suppression suggests that celecoxib is less selective for the inhibition of COX-1 in vivo than preclinical in vitro and ex vivo studies indicate and also suggests that adverse effects attributed to COX-1 suppression may result from celecoxib administration.

AN 2001:110565 BIOSIS
DN PREV200100110565
TI In vivo selectivity of cyclooxygenase-2 inhibitors in the oral surgery model.
AU Khan, A. A. (1); Dionne, R. A.; Capra, N. F.
CS (1) Dental School, Univ. Maryland, Baltimore, MD USA
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-634.9. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience . ISSN: 0190-5295.
DT Conference
LA English
SL English

L12 ANSWER 13 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Cyclooxygenase-2 (**COX-2**) inhibitors constitute a new group of non-steroidal anti-**inflammatory** drugs (NSAIDs) which, at recommended doses, block prostaglandin production by cyclooxygenase-2, but not by cyclooxygenase-1. Two **COX-2** inhibitors are currently available in Australia - celecoxib, which is taken twice daily, and rofecoxib, which is taken once daily. Both drugs act rapidly in providing pain relief and their anti-**inflammatory** analgesic effect in osteoarthritis and rheumatoid arthritis is equivalent to standard doses of non-selective NSAIDs. Celecoxib and rofecoxib show significantly lower incidences of gastrotoxicity (as measured by endoscopic studies and gastrointestinal ulcers and bleeds) than non-selective NSAIDs. There is Level 2 evidence that **COX-2** inhibitors: reduce pain in classic pain models - third-molar

extraction, dysmenorrhoea and after orthopaedic surgery; reduce pain and disability in osteoarthritis of the hip and knee; and reduce pain and disability in rheumatoid arthritis. Other adverse effects, such as interference with antihypertensive agents and the potential to produce renal dysfunction in patients with compromised renal function by **COX-2** inhibitors, seem similar to those of non-selective NSAIDs.

AN 2000:542662 BIOSIS
DN PREV200000542662
TI **COX-2** inhibitors.
AU Brooks, Peter M. (1); Day, Richard O.
CS (1) Faculty of Health Sciences, University of Queensland, Royal Brisbane Hospital, Edith Cavell Building, Herston, QLD, 4029 Australia
SO Medical Journal of Australia, (16 October, 2000) Vol. 173, No. 8, pp. 433-436. print.
ISSN: 0025-729X.
DT Article
LA English
SL English

L12 ANSWER 14 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB The dichloromethane **extract** from the dried flowers of Heterotheca inuloides Cass. was investigated on several pharmacological models of **inflammation** in vivo and in vitro. It showed anti-**inflammatory** activity on the croton oil-induced oedema test in mouse ear, at 1 mg/ear. The compound isolated from this **extract**, 7-hydroxy-3,4-dihydrocadalin, showed anti-**inflammatory** effect on the same experimental model (ED50 of 0.9 mumol/ear), as well as on COX-1 and **COX-2** catalysed prostaglandin biosynthesis assays, with IC50 values of 22 muM and 526 muM, respectively. No effect was observed on carrageenan-induced oedema and on fMLP/PAF-induced exocytosis of human neutrophils. The COX-1 inhibitory effect showed by 7-hydroxy-3,4-dihydrocadalin might be related to the anti-**inflammatory** activity on the topical oedema induced by croton oil.

AN 2000:435463 BIOSIS
DN PREV200000435463
TI Anti-**inflammatory** activity of dichloromethane extract of Heterotheca inuloides in vivo and in vitro.
AU Segura, Laura; Freixa, Blanca; Ringbom, Therese; Vila, Roser; Perera, Premila; Adzet, Tomas; Bohlin, Lars; Canigueral, Salvador (1)
CS (1) Unitat de Farmacologia i Farmacognosia, Facultat de Farmacia, Universitat de Barcelona, Av. Diagonal 643, 08028, Barcelona Spain
SO Planta Medica, (August, 2000) Vol. 66, No. 6, pp. 553-555. print.
ISSN: 0032-0943.
DT Article
LA English
SL English

L12 ANSWER 15 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB The purpose of the present study was to characterize the isoforms of cyclooxygenase (COX) in the human iris before and after stimulation with lipopolysaccharide (LPS) and to determine the selectivity of the nonsteroidal anti-**inflammatory** drug (NSAID), S(+)flurbiprofen, for inhibition of COX-1 and **COX-2** in homogenates of this tissue. Spotblots were made of **extracts** of human iris in the absence and presence of LPS plus acetylsalicylic acid (aspirin). After reacting with anti-COX-1 and anti-**COX-2** immunoglobulin G, the presence of both immunoreactive COX enzymes was substantiated using

an indirect immunoperoxidase method. Authentic COX-1 and **COX-2** were used as controls. Using an enzyme immune assay (EIA), the production of prostaglandin E2 (PGE2) was quantified in tissue homogenates of human iris under the same conditions as described above. S(+)flurbiprofen was added to tissue homogenates in order to determine the inhibitory effect on PGE2 production. Half maximal inhibitory concentrations (IC50) of S(+)flurbiprofen for the PGE2 production in the tissue homogenates were determined from concentration inhibition curves. The selectivity of S(+)flurbiprofen for inhibition of COX-1 was expressed as the ratio of IC50 for **COX-2**/COX-1. Spotblots of nonstimulated iris-**extracts** showed positive staining for COX-1 immunoreactivity (-ir) only. After incubation with LPS plus acetylsalicylic acid, positive staining was observed for both COX-1-ir and **COX-2**-ir. Concentrations of PGE2 released from homogenates of untreated iris varied from 1.5-4 ng/ml, and of LPS-stimulated tissue from 10-20 ng/ml of assay mixture. S(+)flurbiprofen inhibited PGE2 production of untreated tissue homogenates at an IC50 of 8 X 10-10 M whereas, in the stimulated tissue, IC50 was found to be 3 X 10-6 M. The selectivity of S(+)flurbiprofen for inhibition of constitutively present COX-1, relative to the inhibition of induced **COX-2**, was 3,600. Our results indicate that specific expression of COX isoforms in normal human iris was substantiated at the protein level by immunoreaction on spotblots. COX-1 represents the constitutively present enzyme, and **COX-2** appears after stimulation with LPS. At the functional level, S(+)flurbiprofen possesses a specificity for COX-1 in inhibiting PGE2 production.

AN 2000:408492 BIOSIS
DN PREV200000408492
TI Constitutive cyclooxygenase-1 and induced cyclooxygenase-2 in isolated human iris inhibited by S(+)flurbiprofen.
AU van Haeringen, Nicolaas J. (1); van Sorge, Adriaan A.; Carballosa Core-Bodelier, Valerie M. W.
CS (1) Netherlands Ophthalmic Research Institute, 1100 AC, Amsterdam Netherlands
SO Journal of Ocular Pharmacology and Therapeutics, (August, 2000) Vol. 16, No. 4, pp. 353-361. print.
ISSN: 1080-7683.
DT Article
LA English
SL English

L12 ANSWER 16 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB There are about 600 million betel quid (BQ) chewers in the world. BQ chewing is associated with increased incidence of oral cancer and submucous fibrosis. In this study, areca nut (AN) **extract** (200-800 mug/ml) induced the prostaglandin E2 (PGE2) production by 1.4-3.4-fold and 6-keto-PGF1alpha production by 1.1-1.7-fold of gingival keratinocytes (GK), respectively, following 24 h of exposure. Exposure of GK to AN **extract** (>400 mug/ml) led to cell retraction and intracellular vacuoles formation. At concentrations of 800 and 1200 mug/ml, AN **extract** induced cell death at 21-24 and 32-52% as detected by MTT assay and cellular lactate dehydrogenase release, respectively. Interestingly, AN-induced morphological changes of GK are reversible. GK can still proliferate following exposure to AN **extract**. Cytotoxicity of AN **extract** cannot be inhibited by indomethacin (1 muM) and aspirin (50 muM), indicating that

prostaglandin (PG) production is not the major factor responsible for AN cytotoxicity. PGE2 exhibited little effect on the growth of GK at concentrations ranging from 100-1000 pg/ml. Stimulating GK production of PGs by AN **extract** could be due to induction of cyclooxygenase-2 (**COX-2**) mRNA expression and protein production. These results suggest that AN ingredients are critical in the pathogenesis of oral submucous fibrosis and oral cancer via their stimulatory effects on the PGs, **COX-2** production and associated tissue **inflammatory** responses. AN cytotoxicity to GK is not directly mediated by **COX-2** stimulation and PG production.

AN 2000:396530 BIOSIS
DN PREV200000396530
TI Areca nut extract up-regulates prostaglandin production, cyclooxygenase-2 mRNA and protein expression of human oral keratinocytes.
AU Jeng, J. H.; Ho, Y. S.; Chan, C. P.; Wang, Y. J.; Hahn, L. J.; Lei, D.; Hsu, C. C.; Chang, M. C. (1)
CS (1) Team of Biomedical Science, Chang-Gung Institute of Nursing, 261, Wen-Hwa 1 Road, Kwei-Shan, Taoyuan, 33333 Taiwan
SO Carcinogenesis (Oxford), (July, 2000) Vol. 21, No. 7, pp. 1365-1370. print.
ISSN: 0143-3334.
DT Article
LA English
SL English

L12 ANSWER 17 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB This article provides a systematic review of the frequency and severity of adverse gastrointestinal (GI) events among patients using meloxicam, a cyclooxygenase (**COX**)-**2**-selective nonsteroidal anti-**inflammatory** drug (NSAID). A MEDLINE search of English language articles from 1990-1998, a manual search of citations from primary trials and review articles, and a manual search of proceedings from international gastroenterology meetings were conducted. Randomized clinical trials comparing the frequency of GI adverse events for meloxicam versus non-**COX-2**-selective NSAIDs were selected. Specific data about the frequency of dyspepsia; perforations, ulcers, and bleeds (PUBs); and withdrawal of medication because of adverse GI events was also **extracted**. From a pool of 62 potentially relevant citations, 12 randomized trials were identified. All trials concerning symptomatic GI adverse events used the World Health Organization's Adverse Reaction Terminology List (WHO-ARTL) to code adverse events. Patients using meloxicam had fewer GI adverse events compared with non-**COX-2**-selective NSAIDs (odds ratio = 0.64; 95% confidence interval (CI), 0.59-0.69). Patients using meloxicam experienced less dyspepsia (odds ratio = 0.73; 95% CI, 0.64-0.84), fewer PUBs (odds ratio = 0.52; 95% CI, 0.28-0.96), and less frequent discontinuation of NSAID because of adverse GI events (odds ratio = 0.59; 95% CI, 0.52-0.67) compared with non-**COX-2** selective NSAIDs. Meloxicam, a **COX-2**-selective NSAID, appears to cause fewer adverse GI events than standard, non-**COX-2**-selective NSAIDs. However, the generalizability of these data may be limited by the low dose of meloxicam used in most trials and the use of the WHO-ARTL to code adverse events.

AN 2000:199955 BIOSIS
DN PREV200000199955
TI Gastrointestinal safety profile of meloxicam: A meta-analysis and

systematic review of randomized controlled trials.
AU Schoenfeld, Philip (1)
CS (1) Division of Gastroenterology, National Naval Medical Center, 8901 Wisconsin Avenue, Bethesda, MD, 20889 USA
SO American Journal of Medicine, (Dec. 13, 1999) Vol. 107, No. 6 part A, pp. 48S-54S.
ISSN: 0002-9343.
DT Article
LA English
SL English

L12 ANSWER 18 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Objective and Design: We investigated the effect of a new class of **COX-2** inhibitor, rutaecarpine, on the production of PGD2 in bone marrow derived mast cells (BMMC) and PGE2 in **COX-2** transfected HEK293 cells. **Inflammation** was induced by lambda-carrageenan in male Splague-Dawley (SD) rats. Material: Rutaecarpine (8,13-Dihydroindolo(2',3':3,4)pyridol(2,1-b)quinazolin-5(7H)-one) was isolated from the fruits of Evodia rutaecarpa. BMMC were cultured with WEHI-3 conditioned medium. c-Kit ligand and IL-10 were obtained by their expression in baculovirus. Methods: The generation of PGD2 and PGE2 were determined by their assay kit. COX-1 and **COX-2** protein and mRNA expression was determined by BMMC in the presence of KL, LPS and IL-10. Treatment: Rutaecarpine and indomethacin dissolved in 0.1% carboxymethyl cellulose was administered intraperitoneally and, 1 h later, lambda-carrageenan solution was injected to right hind paw of rats. Paw volumes were measured using plethysmometer 5 h after lambda-carrageenan injection. Results: Rutaecarpine inhibited **COX-2** and COX-1 dependent phases of PGD2 generation in BMMC in a concentration-dependent manner with an IC50 of 0.28 muM and 8.7 muM, respectively. It inhibited **COX-2**-dependent conversion of exogenous arachidonic acid to PGE2 in a dose-dependent manner by the **COX-2**-transfected HEK293 cells. However, rutaecarpine inhibited neither PLA2 and COX-1 activity nor **COX-2** protein and mRNA expression up to the concentration of 30 muM in BMMC, indicating that rutaecarpine directly inhibited **COX-2** activity. Furthermore, rutaecarpine showed in vivo anti-**inflammatory** activity on rat lambda-carrageenan induced paw edema by intraperitoneal administration. Conclusion: Anti-**inflammatory** activity of Evodia rutaecarpa could be attributed at least in part by inhibition of COS-2.
AN 2000:100862 BIOSIS
DN PREV200000100862
TI A new class of **COX-2** inhibitor, rutaecarpine from Evodia rutaecarpa.
AU Moon, T. C.; Murakami, M.; Kudo, I.; Son, K. H.; Kim, H. P.; Kang, S. S.; Chang, H. W. (1)
CS (1) College of Pharmacy, Yeungnam University, Gyongsan, 712-749 South Korea
SO Inflammation Research, (Dec., 1999) Vol. 48, No. 12, pp. 621-625.
ISSN: 1023-3830.
DT Article
LA English
SL English

L12 ANSWER 19 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB AIM: The discovery of cyclooxygenase-2 (**COX-2**)

provides a new target for designing nonsteroidal anti-**inflammatory** drugs(NSAIDs) with less side effects. A series of inhibitors were analyzed in order to disclose the relationship between activity and structure. METHODS AND RESULTS: Forty four selective **COX-2** inhibitors were investigated by means of dock and comparative molecular field analysis (CoMFA). Based upon the active conformation **extracted** from the SC-558/**COX-2** complex all inhibitors were docked into receptor and aligned. The model from dock-CoMFA showed higher ability to explain and predict the activity of selective **COX-2** inhibitors, cross-validated Rcv2 = 0.709, non-cross-validated r2 = 0.911, F5,38 = 75.606, SE = 0.242. CONCLUSION: The combination of dock-CoMFA offers an approach to design new molecule.

AN 2000:57130 BIOSIS
DN PREV200000057130
TI Three dimensional quantitative structure-activity relationship of selective cyclooxygenase-2 inhibitors.
AU Lei Xinsheng (1); Zhu Qiqing (1); Qu Lingbo (1); Guo Zongru (1)
CS (1) Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100050 China
SO Yaoxue Xuebao, (1999) Vol. 34, No. 8, pp. 590-595.
ISSN: 0513-4870.
DT Article
LA Chinese
SL Chinese; English

L12 ANSWER 20 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Cyclooxygenase-1 (Cox-1) and **Cox-2** convert arachidonic acid to prostaglandin H2, the precursor of other prostaglandins and thromboxanes, eicosanoids important in vascular pathophysiology. However, knowledge of the expression of cyclooxygenases within atherosclerotic lesions is scant. This study tested the hypothesis that human atheroma and non-atherosclerotic arteries express the two Cox isoforms differentially. Cox-1 mRNA and protein localized on endothelial and medial smooth muscle cells of normal arteries (n = 5), whereas **Cox-2** expression was not detectable. In contrast, atheromatous (n = 7) lesions contained both Cox-1 and **Cox-2**, colocalizing mainly with macrophages of the shoulder region and lipid core periphery, whereas smooth muscle cells showed lower levels, as demonstrated by immunohistochemical and in situ hybridization analysis. Furthermore, microvascular endothelium in plaques showed notable staining for both isoforms. In accord with immunohistochemical studies, Western blot analysis of protein **extracts** from normal arteries revealed constitutive Cox-1, but not **Cox-2**, expression. **Extracts** of atheromatous lesions, however, contained both Cox-1 and **Cox-2** protein, detected as two immunoreactive proteins of approximately 70 and 50 kd. Macrophages expressed the short form of Cox-1/-2 constitutively after several days of in vitro culture, rather than the 70-kd protein. These results shed new light on the **inflammatory** pathways that operate in human atheroma. In particular, the expression of **Cox-2** in atheromatous, but not in unaffected, arteries has therapeutic implications, given the advent of selective **Cox-2** inhibitors.

AN 2000:1638 BIOSIS
DN PREV200000001638
TI Augmented expression of cyclooxygenase-2 in human atherosclerotic lesions.

AU Schonbeck, Uwe; Sukhova, Galina K.; Graber, Pierre; Coulter, Stephanie; Libby, Peter (1)
CS (1) Vascular Medicine and Atherosclerosis Unit, Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, 221 Longwood Avenue, LMRC 307, Boston, MA, 02115 USA
SO American Journal of Pathology, (Oct., 1999) Vol. 155, No. 4, pp. 1281-1291.
ISSN: 0002-9440.
DT Article
LA English
SL English

L12 ANSWER 21 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Atherogenesis involves several aspects of chronic **inflammation** and wound healing. Indeed, the atheroma is considered a special case of tissue response to injury. Injurious stimuli may include lipoproteins trapped within lesions where protein and lipid moieties have undergone chemical modifications. We have studied the effect of oxidized low density lipoproteins (ox-LDL) on inducible cyclooxygenase (**Cox-2**) in human monocyte-derived macrophages exposed to bacterial lipopolysaccharide (LPS). Levels of both **Cox-2** and constitutive cyclooxygenase (Cox-1) were assessed using Western blot analysis. Prior incubation of macrophages with ox-LDL resulted in a strong inhibition of **Cox-2** induced by LPS, without effect on Cox-1. The inhibitory effect was dependent on ox-LDL concentration and its onset was early in time (already detectable 1 hour after macrophage exposure to ox-LDL). Native LDL, and other forms of modified LDL, were without effect. The inhibition was dependent on endocytosis of ox-LDLand could be reproduced using the lipid **extract** from ox-LDL. Lysophosphatidylcholine, 7beta-hydroxycholesterol, and 7-oxocholesterol failed to mimic the inhibition, but oxidized arachidonic acid-containing phospholipids, produced by autoxidation of 1-palmitoyl-2-arachidonoyl-sn-glycero-3-phosphocholine, markedly inhibited **Cox-2**. The observation that ox-LDL downregulates **Cox-2** in human macrophages may explain the fact that, within atheromata, the transformation of macrophages into foam cells results in attenuation of the **inflammatory** response, thus contributing to progression of atherogenesis.
AN 1999:355902 BIOSIS
DN PREV199900355902
TI Oxidized low density lipoprotein suppresses expression of inducible cyclooxygenase in human macrophages.
AU Eligini, Sonia; Colli, Susanna; Basso, Federica; Sironi, Luigi; Tremoli, Elena (1)
CS (1) Institute of Pharmacological Sciences, University of Milan, Via Balzaretti 9, 20133, Milan Italy
SO Arteriosclerosis Thrombosis and Vascular Biology, (July, 1999) Vol. 19, No. 7, pp. 1719-1725.
ISSN: 1079-5642.
DT Article
LA English
SL English

L12 ANSWER 22 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Elevated levels of nitric oxide (NO.) produced by expression of inducible nitric oxide synthase (iNOS/NOS type 2) and high levels of prostaglandins (PGs) generated by expression of inducible cyclooxygenase (**COX-**

2/PGH2 synthase-2) are important mediators of immune and **inflammatory** responses. Previous studies have shown that endogenous levels of NO. can influence the formation of PGs. We examined the mechanism by which NO. regulates PG biosynthesis in macrophages. Treatment of a murine macrophage cell line (ANA-1) with lipopolysaccharide (LPS, 10 ng/mL) and interferon-gamma (IFN-gamma, 10 U/mL) for 20 h elicited high levels of nitrite (NO2-) and prostaglandin E2 (PGE2) that were inhibited in a dose-dependent fashion by the NOS inhibitor, aminoguanidine (AG), with IC50 values of 15.06 and 0.38 muM for NO2- and PGE2, respectively. Stimulation of cultures with LPS and IFN-gamma for 20 h induced de novo iNOS protein expression that was not altered by the addition of AG (0.1, 10, or 1000muM). In contrast, treatment of cultures with LPS and IFN-gamma for 20 h promoted **COX-2** mRNA and protein expression that were decreased in a dose-dependent fashion by AG ($P < 0.05$ with 10 and 1000 muM). LPS and IFN-gamma-induced **COX-2** protein expression was not decreased in cultures treated with AG for 2 h, illustrating that AG does not inhibit the formation of **COX-2** protein. Analysis of partially purified enzyme **extracts** demonstrated that AG did not directly inhibit the enzymatic activity of COX. Additional experiments revealed that NO. donors (S-nitroso-N-aceytl-D-L-pencillamine, SNAP, at 0.1, 10, and 1000 muM) did not induce de novo **COX-2** protein expression or potentiate **COX-2** expression in cells treated with LPS and/or IFN-gamma. Our results suggest that, while endogenous NO. is not required for de novo **COX-2** mRNA and protein expression, NO. is necessary for maintaining prolonged **COX-2** gene expression.

AN 1999:343240 BIOSIS
DN PREV199900343240
TI Blockade of nitric oxide formation down-regulates cyclooxygenase-2 and decreases PGE2 biosynthesis in macrophages.
AU Perkins, Douglas J.; Kniss, Douglas A. (1)
CS (1) Laboratory of Perinatal Research, Department of Obstetrics and Gynecology, Ohio State University, 1654 Upham Drive, Means Hall, Columbus, OH, 43210 USA
SO Journal of Leukocyte Biology, (June, 1999) Vol. 65, No. 6, pp. 792-799. ISSN: 0741-5400.
DT Article
LA English
SL English

L12 ANSWER 23 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Increased expression of cyclooxygenase (COX) and overproduction of prostaglandins (PGs) have been implicated in the development and progression of colorectal cancer (CRC). Nonsteroidal anti-**inflammatory** agents (NSAIDS) inhibit growth of various CRC cell lines by both COX-dependent and COX-independent pathways. To specifically examine the effect of COX and PGs on proliferation in CRC cells, we introduced an antisense **COX-2** cDNA construct under the control of a tetracycline (Tc)-inducible promoter into a CRC cell line, HCA-7, Colony 29 (HCA-7) that expresses COX and produces PGs. In the presence of Tc, PG production in COX-depleted cells was reduced 99.8% compared with either uninduced transfectants or parental HCA-7 cells. This decrease in PG production was associated with a concomitant 60% reduction in DNA replication. Subsequently, we examined the effects of various PGs to modulate cell growth in COX-depleted HCA-7 or COX-null HCT-15 cells by

quantifying (3H)thymidine incorporationand/or growth in collagen gels. We report that J-series cyclopentenone PGs, particularly PGJ2 and 15-deoxy-DELTA12,14-PGJ2, induce proliferation of these cells at nanomolar concentrations. Lipids **extracted** from parental HCA-7 cell conditioned medium stimulated mitogenesis in COX-depleted HCA-7 cells and COX-null HCT-15 cells. Using chromatographic and mass spectrometric approaches, we were able to detect PGJ2 in conditioned medium from parental HCA-7 cells. Taken together, these findings implicate a role for cyclopentenone PGs in CRC cell proliferation.

AN 1999:308544 BIOSIS
DN PREV199900308544
TI Prostaglandin J2 and 15-deoxy-DELTA12,14-prostaglandin J2 induce proliferation of cyclooxygenase-depleted colorectal cancer cells.
AU Chinery, Rebecca; Coffey, Robert J.; Graves-Deal, Ramona; Kirkland, Susan C.; Sanchez, Stephanie C.; Zackert, William E.; Oates, John A.; Morrow, Jason D. (1)
CS (1) Medicine and Pharmacology, Vanderbilt University Medical Center, 506 MRB-1, Nashville, TN, 37232-6602 USA
SO Cancer Research, (June 1, 1999) Vol. 59, No. 11, pp. 2739-2746. ISSN: 0008-5472.
DT Article
LA English
SL English

L12 ANSWER 24 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Two isoforms of cyclooxygenase (COX) have been identified - COX-1, which is constitutively expressed in most tissues, and the inducible form. **COX-2**, of which expression is induced by **inflammatory** signals and mitogens. It has been considered that the beneficial effects of NSAIDs are due to the inhibition of **COX-2** activity and the side effects are from the inhibition of COX-1 activity. Therefore, it is essential to develop selective **COX-2** inhibitor for developing new GI-tolerable NSAIDs. To discover new leads for developing selective **COX-2** inhibitors, three-hundred **extracts** of natural products were primarily screened with the system of prostaglandin accumulation in LPS-stimulated mouse peritoneal macrophages. To identify whether these inhibitory activities of crude **extracts** on the accumulation of prostaglandins were derived from direct action against **COX-2**, the effects of selected **extracts** on exogenous arachidonic acid-derived production of prostaglandins by LPS-stimulated macrophages were determined. Among them, 5 methanol **extracts** of natural products, such as Zingiberis, Rhizoma, Alpinae Officinarum Rhizoma, Caryophilli Flos, Scutellariae Radix, Dalbergia ordorifera, inhibited more than 70% of the prostaglandin production in LPS-stimulated mouse peritoneal macrophages at a concentration of 1 mug/ml.

AN 1999:83024 BIOSIS
DN PREV199900083024
TI Inhibitory activities of natural products on lipopolysaccharide induced prostaglandin production in mouse macrophages.
AU Noh, Min-Soo; Ha, Jun Yong; Lee, Chang Hoon; Lee, Woo Young; Lee, Soo Hwan (1); Lee, Jung Joon
CS (1) Dep. Physiol., Sch. Med., Ajou Univ., Suwon, Kyunggi-Do 442-749 South Korea
SO Yakhak Hoeji, (Dec., 1998) Vol. 42, No. 6, pp. 558-566. ISSN: 0513-4234.
DT Article
LA Korean

SL English

L12 ANSWER 25 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Cyclooxygenase-2 (**COX-2**; EC 1.14-99.1) RNA message abundance in 25 control and Consortium to Establish a Registry for Alzheimer Disease (CERAD)-confirmed sporadic Alzheimer's disease (AD) brains is remarkably heterogeneous when compared with 55 other AD brain RNA message levels that were previously characterized (Lukiw and Bazan: J Neurosci Res 50:937-945, 1997). Examination of nuclear protein **extracts** (NPXTs) that were derived from control and AD-affected brain neocortical nuclei (n = 20; age range, 60-82 years; postmortem interval, 0.5-6.5 hours) by using gel shift, gel supershift, and cold oligonucleotide competition assay revealed a highly significant relationship between the extent of **inflammatory** transcription factor, nuclear factor (NF)-kappaB: DNA binding and the abundance of the **COX-2** RNA signal ($P < 0.0001$; analysis of variance). No strong correlation with AP-1-DNA binding was noted ($P > 0.045$). These data are the first linking **inflammation**-related transcription factor NF-KB-DNA binding to up-regulation of transcription from a key **inflammatory** gene, **COX-2**, in both normally aging brain and in AD-affected neocortex. Systematic deletion of NF-KB-DNA binding sites in human **COX-2** promoter constructs attenuates **COX-2** transcriptional induction by mediators of **inflammation**. Strong NF-KB-DNA binding has been reported previously to temporally precede **COX-2** gene transcription in human epithelial (A549), hamster B-cell (HIT-T15), human endothelial (HUVEC), human lymphoblast (IM9), human fibroblast (IMR90), rat glioma/mouse neuroblastoma (NG108-15), human keratinocyte (NHEK), mouse fibroblast (NIH 3T3), rat neuroblastoma (SH-SY5Y) cell lines and in mouse and rat brain hippocampus, indicating a highly conserved **inflammatory** signaling pathway that is common to diverse species and cell types. The mouse, rat, and human **COX-2** immediate promoters, despite 7.5 X 107 years of DNA sequence divergence, each retain multiple recognition sites specific for NF-KB-DNA binding. These data suggest that basic gene induction mechanisms, which have been conserved over long periods of evolution, that increase NF-KB-DNA binding may be fundamental in driving transcription from **inflammation**-related genes, such as **COX-2**, that operate in stressed tissues, in normally aging cell lines, and in neurodegenerative disorders that include AD brain.
AN 1998:437277 BIOSIS
DN PREV199800437277
TI Strong nuclear factor-kappaB-DNA binding parallels cytlooxygenase-2 gene transcription in aging and in sporadic Alzheimer's disease superior temporal lobe neocortex.
AU Lukiw, Walter J.; Bazan, Nicolas G. (1)
CS (1) Neurosci. Cent., Dep. Ophthalmol., Louisiana State Univ. Sch. Med., New Orleans, LA 70112-2272 USA
SO Journal of Neuroscience Research, (Sept. 1, 1998) Vol. 53, No. 5, pp. 583-592.
ISSN: 0360-4012.
DT Article
LA English

L12 ANSWER 26 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Tissue distributions and association of cyclooxygenase-2 (**COX-2**) with **inflammatory** have led us to search for **COX-2** selective inhibitors from natural products.

Conceptually, **COX-2** selective inhibitors should be expected to retain anti-**inflammatory** efficacy by inhibition of PGs production while reducing or eliminating the gastric, renal and hemostatic side effects commonly associated with NSAIDs use. Thus, a logical approach to the treatment of **inflammatory** diseases should involve the inhibitors of **COX-2**. To develop new **COX-2** inhibitors from natural products, two-hundred crude drugs were screened by inhibiting PGD2 PGD2 generation in bone marrow derived mast cells (BMMC). Among them, 6 methanol **extracts** of crude drugs such as, Bletillae rhizoma, Aconiti koreani rhizoma, Belamcandae rhizoma, Nelumbinis semen, Gleniae radix, Aurantii immatri pericarpium inhibited more than 85% of BMMC **COX-2** activity at a concentration 2.5 mug/ml.

AN 1998:261385 BIOSIS
DN PREV199800261385
TI Screening of cyclooxygenase-2 (**COX-2**) inhibitors from natural products.
AU Moon, Tae Chul (1); Chung, Kyu Charn (1); Son, Kun Ho; Kim, Hyun Pyo; Kang, Sam Sik; Chang, Hyuen Wook
CS (1) Coll. Pharm., Yeungnam Univ., Yeungnam South Korea
SO Yakhak Hoeji, (April, 1998) Vol. 42, No. 2, pp. 214-219. ISSN: 0513-4234.
DT Article
LA Korean; English
SL Korean; English

L12 ANSWER 27 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Objective. **Extracts** of the Chinese herbal remedy Tripterygium wilfordii Hook F (TWHF) have been reported to be effective in the treatment of patients with a variety of **inflammatory** and autoimmune diseases, but the mechanism of this therapeutic effect has not been completely delineated. The present study was designed to assess the effects of TWHF on the in vitro synthesis of prostaglandin E2 (PGE2) and on the expression of the cyclooxygenase isoforms, COX-1 and **COX-2**, in various human cell types. Methods. Monocytes from human peripheral blood (HM), fibroblasts from rheumatoid arthritis synovial tissue (RASF), human neonatal foreskin fibroblasts (HFF), and the histiocytic cell line U937 were cultured for designated time periods with or without lipopolysaccharide (LPS), and in the presence or absence of varying concentrations of the following inhibitors: the methanol/chloroform (T2) **extract** of TWHF, the ethyl acetate (EA) **extract** of TWHF, a purified diterpenoid component of TWHF (triptolide), dexamethasone, and indomethacin. Culture supernatants were harvested for PGE2 content assays. Total RNA was **extracted** from the cells and analyzed for COX-1 and **COX-2** messenger RNA (mRNA) expression using reverse transcriptase polymerase chain reaction or Northern blotting. Results. Both the T2 and EA **extracts** inhibited PGE2 synthesis in the LPS-stimulated HM, RASF, and HFF cells, which was reflected by a marked suppression in the levels of mRNA for **COX-2**. In contrast, neither **extract** inhibited PGE2 production in U937 cells that did not express **COX-2**. Triptolide also inhibited LPS-stimulated induction of **COX-2** mRNA and synthesis of PGE2, at the same inhibitory concentration as seen with the EA **extract**. The effects of T2, EA, and triptolide paralleled the inhibitory action of dexamethasone. Conclusion. The data indicate that both the T2 and EA **extracts** of TWHF, as well as the triptolide component, inhibit PGE2 production in a variety of human cells by blocking the up-regulation of **COX-2**.

AN 1998:170300 BIOSIS
DN PREV199800170300
TI Effects of Tripterygium wilfordii hook F extracts on induction of cyclooxygenase 2 activity and prostaglandin E2 production.
AU Tao, Xuelian; Schulze-Koops, Hendrik; Ma, Li; Cai, Jian; Mao, Yanping; Lipsky, Peter E. (1)
CS (1) Harold C. Simmons Arthritis Res. Cent., Dep. Intern. Med., Univ. Texas Southwestern Med. Cent., 5323 Harry Hines Blvd., Dallas, TX 75235-8884 USA
SO Arthritis & Rheumatism, (Jan., 1998) Vol. 41, No. 1, pp. 130-138. ISSN: 0004-3591.
DT Article
LA English

L12 ANSWER 28 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Objective. Our objective was to characterize the effect of methotrexate (MTX) on prostaglandin E2 (PGE2) synthesis in cultured human rheumatoid synovial cells. Prostaglandins (PG) are important mediators of **inflammation** and joint destruction in rheumatoid arthritis (RA). Two isoforms of cyclooxygenase (COX), the key enzyme in PG synthesis, have been characterized: a constitutively expressed form, COX-1, and an inducible form, **COX-2**. The mechanisms of action of low dose MTX in RA treatment are still poorly understood. As the clinical effects are often first noticed within a month of starting MTX therapy, an antiinflammatory action has been proposed. Methods. Adherent synovial cells were obtained by collagenase digestion of rheumatoid synovium, isolated from patients with RA undergoing synovectomy. Between passages 3 and 6, cultured synovial cells were incubated with or without MTX for 54 h, at various concentrations. Interleukin (IL)-1beta (1 ng/ml) was added or not for the last 6 h of incubation. Supernatants were harvested and assayed for PGE2 by enzyme immunoassay (EIA). Exogenous (1-14C)arachidonic acid metabolism of synoviocytes was analyzed by reverse phase high performance liquid chromatography (RPHPLC). COX-1 and **COX-2** mRNA expression was determined by total RNA **extraction** and reverse transcription polymerase chain reaction. Results. Cellular viability was not affected by MTX. EIA showed that MTX decreased IL-1beta induced PGE2 production by synoviocytes in a dose dependent manner. RP-HPLC analysis confirmed the inhibition of PGE2 and (12S)-12-hydroxy-5,8,10-heptadecatrienoic acid production. COX-1 and IL-1beta induced **COX-2** mRNA expression were not inhibited by MTX.
Conclusion. MTX has an inhibitory effect on IL-1beta stimulated production of PGE2 by cultured human rheumatoid synoviocytes, without affecting either COX mRNA expression. Among various biochemical and immunologic events, MTX could have an antiinflammatory action by decreasing PGE2 release.
AN 1998:161695 BIOSIS
DN PREV199800161695
TI Methotrexate and cyclooxygenase metabolism in cultured human rheumatoid synoviocytes.
AU Vergne, Pascale (1); Liagre, Bertrand; Bertin, Philippe; Cook-Moreau, Jeanne; Treves, Richard; Beneytout, Jean-Louis; Rigaud, Michel
CS (1) Dep. Rheumatol., CHRU Dupuytren, 2 Ave. Martin Luther King, 87042 Limoges Cedex France
SO Journal of Rheumatology, (March, 1998) Vol. 25, No. 3, pp. 433-440. ISSN: 0315-162X.

DT Article
LA English

L12 ANSWER 29 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Etodolac is a non-steroidal anti-**inflammatory** drug with analgesic properties. Its primary antiinflammatory mechanism of action is through a selective effect on cyclo-oxygenase-2 (**COX-2**). It is rapidly absorbed after oral administration, and maximum plasma concentration (C.,) is reached in 12 h, with an elimination half-life (t-1/2) of 6-8 h. Etodolac has been widely applied in the treatment of **inflammatory** arthritides such as rheumatoid arthritis, ankylosing spondylitis and gout and in osteoarthritis and has been shown to be efficacious and well tolerated. However, etodolac has other applications which rely primarily on its efficacy as an analgesic. In particular, etodolac has been evaluated in the treatment of a variety of different pain states. Etodolac has been observed to be efficacious in the treatment of acute pain following dental **extraction**, orthopaedic and urological surgery, and episiotomy, as well as in the treatment of pain due to acute sports injuries, primary dysmenorrhoea, tendonitis, bursitis, periarthritis, radiculalgia and low back pain. These studies indicate that etodolac is a multipurpose analgesic with many clinical applications in addition to its use in the treatment of **inflammatory** and degenerative forms of arthritis.
AN 1997:357139 BIOSIS
DN PREV199799663542
TI Etodolac in the management of pain: A clinical review of a multipurpose analgesic.
AU Bellamy, N.
CS Univ. Western Ontario, London Canada
SO Inflammopharmacology, (1997) Vol. 5, No. 2, pp. 139-152.
ISSN: 0925-4692.
DT General Review
LA English

L12 ANSWER 30 OF 45 BIOSIS COPYRIGHT 2002 BIOSIS
AB Prostaglandin (PG) release, which is increased in vivo by **inflammatory** conditions and in vitro by pro-**inflammatory** cytokines, is decreased by glucocorticoids. Two phospholipase A-2 isoforms, secretory (sPLA-2) and cytosolic (cPLA-2,), have been implicated in **inflammation**. These enzymes catalyse the release of arachidonic acid which is then converted to prostaglandins by the cyclooxygenases (COX-1 and epithelial cells. We have used a human epithelial-like cell line (A549) as a model system to study mRNA expression of sPLA-2, cPLA-2, COX-1 and **COX-2**. Following treatment of cells and **extraction** of RNA, semi-quantitative reverse transcription polymerase chain reaction (RT-PCR) was used to examine expression of these genes. We show a coordinate induction of both cPLA-2 and **COX-2** mRNA by pro-**inflammatory** cytokines which correlated with increased PGE-2 release. By contrast, sPLA-2 mRNA was undetectable and COX-1 was found to be expressed at a constant low level. In addition dexamethasone pretreatment significantly reduced both cPLA-2 and **COX-2** mRNA levels as well as PGE-2 release following cytokine stimulation. These data indicate a major role for control of prostaglandin synthesis at the

mRNA level of key synthetic genes in epithelial cells. Furthermore we show that a major mechanism of glucocorticoid action in preventing prostaglandin release occurs by suppression of cPLA-2 and **COX-2** mRNA levels.

AN 1997:43745 BIOSIS
DN PREV199799335733
TI Cytokine induction of cytosolic phospholipase A-2 and cyclooxygenase-2 mRNA is suppressed by glucocorticoids in human epithelial cells.
AU Newton, R. (1); Kuitert, L. M.; Slater, D. M.; Adcock, I. M.; Barnes, P. J.
CS (1) Dep. Thoracic Med., Natl. Heart Lung Inst., Dovehouse St., London SW3 6LY UK
SO Life Sciences, (1997) Vol. 60, No. 1, pp. 67-78. ISSN: 0024-3205.
DT Article
LA English

L12 ANSWER 31 OF 45 MEDLINE
AB Recently, there have been considerable efforts to search for naturally occurring substances that can inhibit, reverse, or retard the multi-stage carcinogenesis. A wide array of phenolic substances derived from edible and medicinal plants have been reported to possess anticarcinogenic and antimutagenic activities and in many cases, the chemopreventive activities of phytochemicals are associated with their anti-**inflammatory** and/or antioxidative properties. Panax ginseng C.A. Meyer cultivated in Korea has been widely used in traditional herbal medicine for the treatment of various diseases. Certain fractions or purified ingredients of ginseng have been shown to exert anticarcinogenic and antimutagenic activities. Our previous studies have revealed that the methanol **extract** of heat-processed Panax ginseng C.A. Meyer attenuates the lipid peroxidation in rat brain homogenates and is also capable of scavenging superoxide generated by xanthine- xanthine oxidase or by 12-O-tetradecanoylphorbol-13-acetate (TPA) in differentiated human promyelocytic leukemia (HL-60) cells. Topical application of the same **extract** onto shaven backs of female ICR mice also suppressed TPA-induced skin tumor promotion. Likewise, topical application of ginsenoside Rg3, one of the constituents of heat-treated ginseng, significantly inhibited TPA-induced mouse epidermal ornithine decarboxylase activity and skin tumor promotion. Expression of cyclooxygenase-2 (**COX-2**) in TPA-stimulated mouse skin was markedly suppressed by Rg3 pretreatment. In addition, Rg3 inhibited TPA-stimulated activation of NF-kB and extracellular-regulated protein kinase (ERK), one of the mitogen-activated protein (MAP) kinase in mouse skin and also in cultured human breast epithelial cells (MCF-10A).
AN 2001700103 IN-PROCESS
DN 21615193 PubMed ID: 11748375
TI Molecular Mechanisms Underlying Anti-Tumor Promoting Activities of Heat-Processed Panax ginseng C.A. Meyer.
AU Surh Y J; Na H K; Lee J Y; Keum Y S
CS College of Pharmacy, Seoul National University, Seoul, Korea.. surh@plaza.snu.ac.kr
SO JOURNAL OF KOREAN MEDICAL SCIENCE, (2001 Dec) 16 Suppl S38-41. Journal code: AH4; 8703518. ISSN: 1011-8934.
CY Korea (South)
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20011219

Last Updated on STN: 20011219

L12 ANSWER 32 OF 45 MEDLINE
AB An **inflammatory** response accompanies the reversible pneumotoxicity caused by butylated hydroxytoluene (BHT) administration to mice. Lung tumor formation is promoted by BHT administration following an initiating agent in BALB/cByJ mice, but not in CXB4 mice. To assess the contribution of **inflammation** to this differential susceptibility, we quantitatively characterized **inflammation** after one 150 mg/kg body weight, followed by three weekly 200 mg/kg ip injections of BHT into male mice of both strains. This examination included **inflammatory** cell infiltrate and protein contents in bronchoalveolar lavage (BAL) fluid, cyclooxygenase (COX)-1 and **COX-2** expression in lung **extracts**, and PGE(2) and PGI(2) production by isolated bronchiolar Clara cells. BAL macrophage and lymphocyte numbers increased in BALB mice ($P<0.0007$ and 0.02, respectively), as did BAL protein content ($P<0.05$), COX-1 and **COX-2** expression ($P<0.05$ for each), and PGI(2) production ($P<0.05$); conversely, these indices were not perturbed by BHT in CXB4 mice. BALB mice fed aspirin (400 mg/kg of chow) for two weeks prior to BHT treatment had reduced **inflammatory** cell infiltration. Our results support a hypothesis that resistance to BHT-induced **inflammation** in CXB4 mice accounts, at least in part, for the lack of effect of BHT on lung tumor multiplicity in this strain.
AN 2001644493 IN-PROCESS
DN 21553648 PubMed ID: 11696405
TI The lung tumor promoter, butylated hydroxytoluene (BHT), causes chronic **inflammation** in promotion-sensitive BALB/cByJ mice but not in promotion-resistant CXB4 mice.
AU Bauer A K; Dwyer-Nield L D; Hankin J A; Murphy R C; Malkinson A M
CS Department of Pharmacology, University of Colorado Health Sciences Center, 80262, Denver, CO, USA.
SO TOXICOLOGY, (2001 Dec 1) 169 (1) 1-15.
Journal code: VWR; 0361055. ISSN: 0300-483X.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20011107
Last Updated on STN: 20011107

L12 ANSWER 33 OF 45 MEDLINE
AB OBJECTIVE: Various **extracts** of the Chinese herbal remedy Tripterygium wilfordii Hook. f. (TWHF) have been reported to be therapeutically efficacious in rheumatoid arthritis (RA) in China, but their mechanism of action remains unclear. We investigated the effect of triptolide, a diterpenoid triepoxide from TWHF, on the production of pro-matrix metalloproteinase 1 (proMMP-1; or procollagenase 1 or pro-interstitial collagenase 1), proMMP-3 (or prostromelysin 1), tissue inhibitors of metalloproteinases (TIMPs), and proinflammatory cytokines in human synovial fibroblasts and J774A.1 mouse macrophages. METHODS: Human synovial fibroblasts and mouse macrophages were cultured with interleukin-1alpha (IL-1alpha) or lipopolysaccharide (LPS) in the presence or absence of triptolide. The production of proMMPs 1 and 3, TIMPs 1 and 2, cyclooxygenase 1 (COX-1) and **COX-2**, prostaglandin E2 (PGE2), IL-1beta, and IL-6 was assayed by Western blot analysis and enzyme-linked immunosorbent assay. Gene expression of proMMPs 1 and 3,

TIMPs 1 and 2, COX-1 and **COX-2**, IL-1alpha, IL-1beta, tumor necrosis factor alpha (TNFalpha), and IL-6 was also monitored by Northern blot analysis and reverse transcriptase-polymerase chain reaction. RESULTS: Triptolide suppressed the IL-1alpha-induced production of proMMPs 1 and 3 and decreased their messenger RNA levels in human synovial fibroblasts. In contrast, the IL-1alpha-induced gene expression and production of TIMPs 1 and 2 were further augmented by triptolide in the synovial cells. Triptolide also inhibited the IL-1alpha-induced production of PGE2 by selectively suppressing the gene expression and production of **COX-2**, but not those of COX-1. In addition, triptolide suppressed the LPS-induced production of PGE2 in mouse macrophages. Furthermore, the gene expression of IL-1alpha, IL-1beta, TNFalpha, and IL-6, as well as the production of IL-1beta and IL-6, were inhibited by triptolide in the LPS-treated mouse macrophages. CONCLUSION: We have demonstrated for the first time that the therapeutic effects of TWHF in RA are due in part to the novel chondroprotective effect of triptolide via the direct suppression of the production of proMMPs 1 and 3 and the simultaneous up-regulation of TIMPs in IL-1-treated synovial fibroblasts. Triptolide's interference with gene expression of proinflammatory cytokines and its known inhibitory effects on PGE2 production are also probably very effective.

AN 2001545814 MEDLINE
DN 21476380 PubMed ID: 11592385
TI Triptolide, a novel diterpenoid triepoxide from Tripterygium wilfordii Hook. f., suppresses the production and gene expression of pro-matrix metalloproteinases 1 and 3 and augments those of tissue inhibitors of metalloproteinases 1 and 2 in human synovial fibroblasts.
AU Lin N; Sato T; Ito A
CS Institute of Chinese Materia Medica, China Academy of Traditional Chinese Medicine, Beijing.
SO ARTHRITIS AND RHEUMATISM, (2001 Sep) 44 (9) 2193-200.
Journal code: 90M; 0370605. ISSN: 0004-3591.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200111
ED Entered STN: 20011011
Last Updated on STN: 20011105
Entered Medline: 20011101

L12 ANSWER 34 OF 45 MEDLINE
AB Characteristics of cyclooxygenase-2 (**COX-2**) expressing cells in human dental pulp were immunohistologically studied. Extirpated pulpal tissues from **extracted** teeth were examined to elucidate the localization and distribution of **COX-2**. Pulpal tissues were examined by the labeled streptavidin biotin method using specific mouse monoclonal antibodies for **COX-2**. Cell types of the **COX-2** expressing cells were also investigated by the double stain technique using both monoclonal antibodies for CD68/macrophage and anti-**COX-2**. **COX-2** expressing cells could be found in all of the inflamed pulps, and these cells were mostly distributed close to the area of accumulation of **inflammatory** cells. **COX-2** was mainly expressed in fibroblasts rather than macrophages. In contrast, **COX-2** expressing cells were scarcely found in the normal pulps. These findings indicate that pulpal fibroblasts, as well as macrophages, may participate in the production of prostaglandin through **COX-2** expression in pulpal **inflammation**, and might be involved in the pathogenesis of irreversible pulpitis.

AN 2001440527 MEDLINE
DN 21379249 PubMed ID: 11487130
TI An immunohistological study on cyclooxygenase-2 in human dental pulp.
AU Nakanishi T; Shimizu H; Hosokawa Y; Matsuo T
CS Department of Conservative Dentistry, School of Dentistry, The University of Tokushima, Japan.
SO JOURNAL OF ENDODONTICS, (2001 Jun) 27 (6) 385-8.
Journal code: I1K; 7511484. ISSN: 0099-2399.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Dental Journals
EM 200111
ED Entered STN: 20010813
Last Updated on STN: 20011105
Entered Medline: 20011101

L12 ANSWER 35 OF 45 MEDLINE
AB OBJECTIVE: To examine the cellular mechanisms involved in the pathogenesis of necrotizing enterocolitis (NEC). SUMMARY BACKGROUND DATA: Necrotizing enterocolitis is a major cause of death and complications in neonates; the cellular mechanisms responsible for NEC are unknown. The inducible form of cyclooxygenase (i.e., **COX-2**) is activated by the transcription factor nuclear factor (NF)-kappaB and is thought to play a role in **inflammation**. METHODS: Segments of perforated and adjacent uninvolved small intestine from neonates with NEC were analyzed for **COX-2** expression by immunohistochemistry. NEC was induced in weanling (18 days old) rats by occlusion of superior mesenteric vessels for 1 hour and intraluminal injection of platelet activating factor (50 micro/kg). Small intestine was harvested for protein **extraction**. Western immunoblot was performed to determine expression of **COX-2**. Gel shift assays were performed to assess NF-kappaB binding activity. RESULTS: Immunohistochemical analysis showed increased **COX-2** protein expression in the perforated intestinal sections of all 36 neonates but not in adjacent normal intestine. Increased expression of **COX-2** protein and NF-kappaB binding activity was noted in the small intestine of weanling rats at 0 and 3 hours after induction of NEC. CONCLUSIONS: Increased **COX-2** expression was identified in all neonatal intestinal segments resected for perforated NEC. In addition, a coordinate induction of **COX-2** expression and NF-kappaB binding was noted in a rodent model of NEC. These findings suggest that the **COX-2**/NF-kappaB pathway may play a role in the pathogenesis of NEC. Therapeutic agents that target this pathway may prove useful in the treatment or possible prevention of NEC.
AN 2001277577 MEDLINE
DN 21264028 PubMed ID: 11371742
TI Molecular mechanisms contributing to necrotizing enterocolitis.
AU Chung D H; Ethridge R T; Kim S; Owens-Stovall S; Hernandez A; Kelly D R; Evers B M
CS Department of Surgery, The University of Texas Medical Branch, Galveston, Texas 77555-0353, USA.. dhchung@utmb.edu
NC PO1 DK35608 (NIDDK)
RO1 DK48498 (NIDDK)

T32 DK07639 (NIDDK)
SO ANNALS OF SURGERY, (2001 Jun) 233 (6) 835-42.
Journal code: 67S; 0372354. ISSN: 0003-4932.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200106
ED Entered STN: 20010625
Last Updated on STN: 20010625
Entered Medline: 20010621

L12 ANSWER 36 OF 45 MEDLINE
AB Rhizoma Cimicifugae (RC) has been used traditionally to treat pain and **inflammation** in Korea. The present study was conducted to gain insights into the mechanism of action regarding analgesic and antiinflammatory activities of RC extracts. RC was first extracted with methanol. The methanol extract (A) was fractionated to an ether-soluble fraction (B) and a water-soluble fraction (C). Fraction C was fractionated to a butanol-soluble fraction (D) and a water-soluble fraction (E). Each fraction (100 mg/kg, i.p.) was tested for analgesic and antiinflammatory activities. Administration of fractions A and D caused dramatic analgesic effects based on acetic acid writhing and tail-flick assays. However, fraction E had an analgesic effect only based on the acetic acid writhing assay. Fractions A, D and E exerted antiinflammatory effects on the rat paw oedema assay. The fractions A, D, E had an inhibitory action on the bradykinin/histamine-mediated contractions of guinea-pig ileum. In addition, fractions A, D and E had the ability to inhibit the production of LPS-induced 6-keto-PGF1alpha production in macrophage cultures. Taken together, these results provide scientific evidence that RC extracts exert analgesic and antiinflammatory effects by inhibiting bradykinin/histamine mediated actions and inhibiting 6-keto-PGF1alpha induction.
AN 2001176499 MEDLINE
DN 20566070 PubMed ID: 11113994
TI Inhibitory effects of cimicifugae rhizoma **extracts** on histamine, bradykinin and **COX-2** mediated **inflammatory** actions.
AU Kim S J; Kim M S
CS Department of Pharmacology, School of Dentistry and Institute of Oral Biology, Kyung Hee University, Seoul, Korea 130-701.. kimsj@nms.kyunghee.ac.kr
SO PHYTOTHERAPY RESEARCH, (2000 Dec) 14 (8) 596-600.
Journal code: C6Y; 8904486. ISSN: 0951-418X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010329

L12 ANSWER 37 OF 45 MEDLINE
AB OBJECTIVE: To discern the effects of continuous passive motion on inflamed temporomandibular joints (TMJ). METHODS: The effects of continuous passive motion on TMJ were simulated by exposing primary cultures of rabbit TMJ

fibrochondrocyte monolayers to cyclic tensile strain (CTS) in the presence of recombinant human interleukin-1beta (rHuIL-1beta) in vitro. The messenger RNA (mRNA) induction of rHuIL-1beta response elements was examined by semiquantitative reverse transcriptase-polymerase chain reaction. The synthesis of nitric oxide was examined by Griess reaction, and the synthesis of prostaglandin E2 (PGE2) was examined by radioimmunoassay. The synthesis of proteins was examined by Western blot analysis of the cell **extracts**, and synthesis of proteoglycans via incorporation of 35S-sodium sulfate in the culture medium. RESULTS: Exposure of TMJ fibrochondrocytes to rHuIL-1beta resulted in the induction of inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (**COX-2**), which were paralleled by NO and PGE2 production. Additionally, IL-1beta induced significant levels of collagenase (matrix metalloproteinase 1 [MMP-1]) within 4 hours, and this was sustained over a period of 48 hours. Concomitant application of CTS abrogated the catabolic effects of IL-1beta on TMJ chondrocytes by inhibiting iNOS, **COX-2**, and MMP-1 mRNA production and NO, PGE2, and MMP-1 synthesis. CTS also counteracted cartilage degradation by augmenting expression of mRNA for tissue inhibitor of metalloproteinases 2 that is inhibited by rHuIL-1beta. In parallel, CTS also counteracted rHuIL-1beta-induced suppression of proteoglycan synthesis. Nevertheless, the presence of an **inflammatory** signal was a prerequisite for the observed CTS actions, because fibrochondrocytes, when exposed to CTS alone, did not exhibit any of the effects described above. CONCLUSION: CTS acts as an effective antagonist of rHuIL-1beta by potentially diminishing its catabolic actions on TMJ fibrochondrocytes. Furthermore, CTS actions appear to involve disruption/regulation of signal transduction cascade of rHuIL-1beta upstream of mRNA transcription.

AN 2001163838 MEDLINE
DN 21161187 PubMed ID: 11263775
TI Cyclic tensile strain suppresses catabolic effects of interleukin-1beta in fibrochondrocytes from the temporomandibular joint.
CM Comment on: Arthritis Rheum. 2001 Mar;44(3):666-75
AU Agarwal S; Long P; Gassner R; Piesco N P; Buckley M J
CS University of Pittsburgh, Pennsylvania, USA.
NC R-15-DE-12976 (NIDCR)
SO ARTHRITIS AND RHEUMATISM, (2001 Mar) 44 (3) 608-17.
Journal code: 90M; 0370605. ISSN: 0004-3591.
CY United States
DT Commentary
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200105
ED Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010503

L12 ANSWER 38 OF 45 MEDLINE

AB The dichloromethane **extract** from the dried flowers of Heterotheca inuloides Cass. was investigated on several pharmacological models of **inflammation** in vivo and in vitro. It showed anti-**inflammatory** activity on the croton oil-induced oedema test in mouse ear, at 1 mg/ear. The compound isolated from this **extract**, 7-hydroxy-3,4-dihydrocadalin, showed anti-**inflammatory** effect on

the same experimental model (ED50 of 0.9 mumol/ear), as well as on COX-1 and **COX-2** catalysed prostaglandin biosynthesis assays, with IC50 values of 22 microM and 526 microM, respectively. No effect was observed on carrageenan-induced oedema and on fMLP/PAF-induced exocytosis of human neutrophils. The COX-1 inhibitory effect showed by 7-hydroxy-3,4-dihydrocadalin might be related to the anti-**inflammatory** activity on the topical oedema induced by croton oil.

AN 2000498031 MEDLINE
DN 20441099 PubMed ID: 10985084
TI Anti-**inflammatory** activity of dichloromethane extract of Heterotheca inuloides in vivo and in vitro.
AU Segura L; Freixa B; Ringbom T; Vila R; Perera P; Adzet T; Bohlin L; Canigueral S
SO PLANTA MEDICA, (2000 Aug) 66 (6) 553-5.
Journal code: P9F; 0066751. ISSN: 0032-0943.
CY GERMANY: Germany, Federal Republic of
DT Letter
LA English
FS Priority Journals
EM 200010
ED Entered STN: 20001027
Last Updated on STN: 20001027
Entered Medline: 20001018

L12 ANSWER 39 OF 45 MEDLINE
AB Even at the beginning of the next millennium, aspirin will still offer surprises. Its relatively young pharmacological history compares with the early use of salicylate-containing plants since antiquity. The Assyrians and the Egyptians were aware of the analgesic effects of a decoction of myrtle or willow leaves for joint pains. Hippocrates recommended chewing willow leaves for analgesia in childbirth and the Reverend Edward Stones is acknowledged as the first person to scientifically define the beneficial antipyretic effects of willow bark. At the beginning of the 19th century salicin was **extracted** from willow bark and purified. Although a French chemist, Charles Gerhardt, was the first to synthesize aspirin in a crude form, the compound was ignored, and later studied by Felix Hoffmann. He reportedly tested the rediscovered agent on himself and on his father, who suffered from chronic arthritis--a legend was born and Bayer Laboratories rose to the heights of the pharmacological world. First used for its potent analgesic, antipyretic and anti-**inflammatory** properties, aspirin was successfully used as an antithrombotic agent. Sir John Vane elucidated aspirin's active mechanism as an inhibitor of prostaglandin synthetase and received the Nobel Price in Medicine for this work in 1982. Two isoform of cyclooxygenase (COX-1 and **COX-2**) have now been identified, each possessing similar activities, but differing in characteristic tissue expression. The cox enzyme is now a target of drug interventions against the **inflammatory** process. After two centuries of evaluation, aspirin remains topical, and new therapeutic indications are increasingly being studied.

AN 2000226410 MEDLINE
DN 20226410 PubMed ID: 10763200
TI [Aspirin throughout the ages: a historical review].
L'aspirine a travers les siecles: rappel historique.
AU Levesque H; Lafont O
CS Departement de medecine interne, centre hospitalier universitaire Rouen-Boisguillaume, France.
SO REVUE DE MEDECINE INTERNE, (2000 Mar) 21 Suppl 1 8s-17s. Ref: 54

Journal code: SGJ; 8101383. ISSN: 0248-8663.
CY France
DT Historical
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA French
FS Priority Journals
EM 200004
ED Entered STN: 20000505
Last Updated on STN: 20000505
Entered Medline: 20000427

L12 ANSWER 40 OF 45 MEDLINE
AB OBJECTIVE: Several **extracts** of Tripterygium wilfordii Hook F (TWHF) have been reported to be effective in patients with rheumatoid arthritis. We investigated the effect of multi-glycosides ofTWHF (GTW), a TWHF **extract**, on interleukin (IL)-1beta stimulated human rheumatoid synovial cells. MATERIALS AND METHODS: IL-1beta-stimulated synovial cells were used to detect the effects of GTW on cyclooxygenase (COX)-1 and **COX-2** activities, expression of COX protein and mRNA, and nuclear transcription factors in experiments using respective reporter plasmids. RESULTS: GTW inhibited prostaglandin E2 production by IL-1beta-stimulated synovial cells in a concentration-dependent manner, and also inhibited **COX-2** protein and mRNA expression in a similar fashion to dexamethasone. However, GTW did not act as a glucocorticoid agonist. GTW repressed IL-1beta-induced nuclear factor-kappaB activity, but did not have a significant influence on activating protein-1 activity. CONCLUSION: The anti-rheumatic effect of GTW or TWHF may be partly mediated through the inhibition of prostaglandin E2 production in human synovial cells due to suppression of **COX-2** mRNA, possibly via inhibition of nuclear factor-kappaB activity.
AN 2000064883 MEDLINE
DN 20064883 PubMed ID: 10598013
TI The molecular mechanism of inhibition of interleukin-1beta-induced cyclooxygenase-2 expression in human synovial cells by Tripterygium wilfordii Hook F extract.
AU Maekawa K; Yoshikawa N; Du J; Nishida S; Kitasato H; Okamoto K; Tanaka H; Mizushima Y; Kawai S
CS Institute of Medical Science, St Marianna University School of Medicine, Miyamae, Kawasaki, Japan.
SO INFLAMMATION RESEARCH, (1999 Nov) 48 (11) 575-81.
Journal code: B8U; 9508160. ISSN: 1023-3830.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200001
ED Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000124

L12 ANSWER 41 OF 45 MEDLINE
AB Celecoxib offers the unique therapeutic prospect of alleviating pain and **inflammation** without the untoward gastrointestinal, renal, and platelet effects associated with conventional nonsteroidal anti-**inflammatory** drugs. This is possible because celecoxib is a cyclooxygenase-2 (**COX-2**)-specific inhibiting agent

that inhibits the conversion of arachidonic acid to the prostaglandins that mediate pain and **inflammation** while having no effect on the formation of the prostaglandins that mediate normal homeostasis in the gastrointestinal tract, kidneys, and platelets and that are formed under the control of cyclooxygenase-1 (COX-1). Double-blind clinical trials have demonstrated that celecoxib is as effective in ameliorating the signs and symptoms of osteoarthritis and rheumatoid arthritis as naproxen and as effective as aspirin in reducing pain following dental **extraction**. Controlled trials have also shown that the incidence of gastroduodenal ulcers and the combined incidence of gastroduodenal ulcers and erosions are significantly lower with celecoxib therapy than with naproxen therapy and are similar to those associated with placebo administration. In a study of platelet function, it was found that a single 650-mg dose of aspirin profoundly diminished platelet function, while therapeutic doses of celecoxib exhibited no such effect. Celecoxib has been shown to be well tolerated, with incidences of adverse events similar to placebo in most instances. In summary, evidence to date indicates that celecoxib is a safe and effective therapeutic modality for the management of arthritis and pain.

AN 1999208341 MEDLINE
DN 99208341 PubMed ID: 10193998
TI Celecoxib, a **COX-2**--specific inhibitor: the clinical data.
AU Fort J
CS Medical Affairs, G.D. Searle & Co, Skokie, Illinois, USA.
SO AMERICAN JOURNAL OF ORTHOPEDICS, (1999 Mar) 28 (3 Suppl) 13-8. Ref: 14
Journal code: B41; 9502918. ISSN: 1078-4519.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 19990601
Last Updated on STN: 20000303
Entered Medline: 19990519

L12 ANSWER 42 OF 45 MEDLINE
AB Nimesulide is a selective **COX-2** inhibitor used in a variety of **inflammatory**, pain and fever states. After healthy volunteers received oral nimesulide 100 mg in tablet, granule or suspension form the drug was rapidly and extensively absorbed. Mean peak concentrations (Cmax) of 2.86 to 6.50 mg/L were achieved within 1.22 to 2.75 hours of administration. The presence of food did not reduce either the rate or extent of nimesulide absorption. When nimesulide was administered in the suppository form, the Cmax was lower and occurred later than after oral administration; the bioavailability of nimesulide via suppository ranged from 54 to 64%, relative to that of orally administered formulations. Nimesulide is rapidly distributed and has an apparent volume of distribution ranging between 0.18 and 0.39 L/kg. It is extensively bound to albumin; the unbound fraction in plasma was 1%. The unbound fraction increased to 2 and 4% in patients with renal or hepatic insufficiency. With oral administration, the concentrations of nimesulide declined monoexponentially following Cmax. The estimated mean terminal elimination half-life varied from 1.80 to 4.73 hours. Excretion of the unchanged drug in urine and faeces is negligible. Nimesulide is largely

eliminated via metabolic transformation and the principal metabolite is the 4'-hydroxy derivative (M1). Minor metabolites have been detected in urine and faeces, mainly in a conjugated form. Pharmacological tests in vivo have shown that the metabolites are endowed with anti-**inflammatory** and analgesic properties, although their activity is lower than that of nimesulide. Excretion in the urine and faeces accounted for 50.5 to 62.5% and 17.9 to 36.2% of an orally administered dose, respectively. The total plasma clearance of nimesulide, was 31.02 to 106.16 ml/h/kg, reflecting almost exclusive metabolic clearance. The drug has a low **extraction** ratio, close to 0.1. With twice daily oral or rectal administration of nimesulide, steady-state was achieved within 24 to 48 hours (2 to 4 administrations); only modest accumulation of nimesulide and M1 occurred. Gender has only a limited influence on the pharmacokinetic profiles of nimesulide and M1. The pharmacokinetic profiles of nimesulide and M1 in children and the elderly did not differ from that of healthy young individuals. Hepatic insufficiency affected the pharmacokinetics of nimesulide and M1 to a significant extent: the rate of elimination of nimesulide and M1 was remarkably reduced in comparison to the rate of elimination in healthy individuals. Therefore, a dose reduction (4 to 5 times) is required in patients with hepatic impairment. The pharmacokinetic profile of nimesulide and M1 was not altered in patients with moderate renal failure and no dose adjustment in patients with creatinine clearances higher than 1.8 L/h is envisaged. Pharmacokinetic interactions between nimesulide and other drugs given in combination [i.e. glibenclamide, cimetidine, antacids, furosemide (frusemide), theophylline, warfarin and digoxin] were absent, or of no apparent clinical relevance.

AN 1999028711 MEDLINE
DN 99028711 PubMed ID: 9812177
TI Clinical pharmacokinetics of nimesulide.
AU Bernareggi A
CS Department of Pharmacokinetics and Biochemistry, Research Centre, Monza, Italy.. alberto_bernareggi@bmg.boehringer-mannheim.com
SO CLINICAL PHARMACOKINETICS, (1998 Oct) 35 (4) 247-74. Ref: 94
Journal code: DG5; 7606849. ISSN: 0312-5963.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199901
ED Entered STN: 19990209
Last Updated on STN: 20000303
Entered Medline: 19990122

L12 ANSWER 43 OF 45 MEDLINE
AB Although the severity of periodontal disease is known to be affected by age, functional changes of periodontal tissue cells during the aging process are not well characterized. It is important to define how cellular aging affects the progression of periodontal diseases associated with the aging process. In vitro aging of human gingival fibroblast (HGF) and periodontal ligament fibroblast (HPLF) cells was prepared by sequential subcultivations (5 to 6 passages as young, 18 to 20 passages as old). GFs were also prepared from gingiva of Down's syndrome patients and 60-week-old rats. Fetal rat calvarial osteoblasts were prepared by

sequential digestion with collagenase. HGF and HPLF cells were treated with lipopolysaccharide (LPS) and cyclic tension force, respectively. Amounts of PGE2, interleukin (IL)-1 beta, IL-6, and plasminogen activator (PA) in conditioned media were measured. Total RNA was **extracted**, and mRNA expression was analyzed by reverse transcription polymerase chain reaction (RT-PCR). LPS-stimulated PGE2, IL-1 beta, IL-6, and PA production was increased in "old" HGF compared to younger cells. According to RT-PCR analysis, gene expression of **COX-2**, IL-1 beta, IL-6, and tissue type (t) PA was higher in old cells than in young cells. Cyclic tension force to HPLF also stimulated phenotypic and gene expression of IL-1 beta, PGE2 (**COX-2** gene) and tPA. These findings suggest that aging in both HGF and HPLF may be an important factor in the severity of periodontal disease through higher production of **inflammatory** mediators in response to both LPS and mechanical stress. In addition, oxygen radical-treated fibronectin (FN) as substratum diminished bone nodule formation by osteoblasts when compared with intact FN. This finding suggests that FN plays an important role in Osteoblast activity and that FN damaged by oxygen radicals during the aging process may be related to less bone formation.

AN 1998389943 MEDLINE
DN 98389943 PubMed ID: 9722719
TI Effect of aging on functional changes of periodontal tissue cells.
AU Abiko Y; Shimizu N; Yamaguchi M; Suzuki H; Takiguchi H
CS Department of Biochemistry, Nihon University School of Dentistry at Matsudo, Chiba, Japan.. yabiko@mascat.nihon-u.ac.jp
SO ANNALS OF PERIODONTOLOGY, (1998 Jul) 3 (1) 350-69.
Journal code: CTP; 9702874.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Dental Journals
EM 199809
ED Entered STN: 19980910
Last Updated on STN: 19980910
Entered Medline: 19980903

L12 ANSWER 44 OF 45 MEDLINE
AB 1. The responses of wide dynamic range spinal dorsal horn neurones to noxious mechanical stimulation of the ankle or knee joint were tested before and after spinal administration of the non-selective cyclooxygenase (COX) inhibitors, indomethacin and meclofenamic acid. Neither of these drugs altered the responses of these neurones to noxious mechanical stimulation. 2. Wind-up of a spinal nociceptive reflex evoked by electrical stimulation of the sural nerve at C-fibre strength was dose-dependently inhibited by intravenous administration of indomethacin, a non-selective COX inhibitor, and SC58125, a selective **COX-2** inhibitor. Intrathecal administration of indomethacin also reduced the wind-up of this nociceptive reflex. 3. Western blot analysis of proteins **extracted** from normal rat spinal cord revealed the presence of both cyclo-oxygenase (COX)-1 and **COX-2** proteins. 4. Immunocytochemistry of sections of normal rat spinal cord with specific COX-1 antiserum revealed little specific COX-1-like immunoreactivity in the grey matter. With the same antiserum, intense COX-1-like immunoreactivity was observed in the cytoplasm, nuclear membrane and axonal processes of small to medium sized (< 1000 microns2)

dorsal root ganglion (DRG) cell bodies. 5. Immunocytochemistry of sections of normal rat spinal cord incubated with specific **COX-2** antiserum showed intense **COX-2**-like immunoreactivity (**COX-2**-li) in the superficial dorsal horn of the spinal cord (laminae I and II) and around the central canal (lamina X). **COX-2**-li was also observed in some neurones in deep dorsal horn and in individual motor neurones in ventral horn. **COX-2**-li was not observed in the cell bodies of DRG. 6. Superfusion of the lumbar spinal cord of normal rats with artificial CSF and subsequent radioimmunoassay revealed the presence of prostaglandin D2 (PGD2) < PGE2, but not PGI2 (determined by measurement of the stable metabolite, 6-keto-PGF1 alpha) or PGF2 alpha. 7. These data suggest that eicosanoids synthesized by an active COX pathway in the spinal cord of normal animals may contribute to nociceptive processing, but only when the spinal cord neurones are rendered hyperexcitable following C-fibre stimulation. Selective inhibition of one or both of the COX isoforms in normal animals may represent a novel target for spinal analgesia.

AN 1998084781 MEDLINE
DN 98084781 PubMed ID: 9422803
TI Prostanoids synthesized by cyclo-oxygenase isoforms in rat spinal cord and their contribution to the development of neuronal hyperexcitability.
AU Willingale H L; Gardiner N J; McLymont N; Giblett S; Grubb B D
CS Department of Cell Physiology and Pharmacology, University of Leicester.
SO BRITISH JOURNAL OF PHARMACOLOGY, (1997 Dec) 122 (8) 1593-604.
Journal code: B00; 7502536. ISSN: 0007-1188.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199801
ED Entered STN: 19980206
Last Updated on STN: 19980206
Entered Medline: 19980128

L12 ANSWER 45 OF 45 MEDLINE
AB Tumour necrosis factor-alpha (TNF-alpha) is a pleiotropic cytokine which stimulates the synthesis and release of prostaglandins (PGs) in several in vitro and in vivo models of preterm labour. While TNF-alpha simulated PG production has been described in decidual, amnion and myometrial cells, to date no studies have focused on the role of TNF-alpha in the stimulation of arachidonic acid metabolism in placental trophoblast cells. Cyclo-oxygenase-2 (**COX-2**) is the rate-limiting enzyme in PG biosynthesis and is expressed de novo during cellular activation by cytokines. To test whether TNF-alpha alters expression of **COX-2**, trophoblasts from first trimester chorionic vili were cultured as a continuous cell line and treated with TNF-alpha alone or with TNF-alpha and dexamethasone (Dex). Total RNA and protein were **extracted** from the trophoblasts and subjected to Northern and immunoblot analysis, respectively. Northern blots were hybridized with a 32P-labelled probe encoding the **COX-2** cDNA and immunoblots were incubated with anti-**COX-2** antibodies. There was a time- and dose-dependent increase in **COX-2** mRNA and protein expression in cells stimulated with TNF-alpha. The effect of TNF-alpha on **COX-2** mRNA and protein expression was

inhibited by dexamethasone (Dex). To examine the production of PGE2 and PGF(2 alpha), specific RIAs were performed on culture media from similarly stimulated cells. PG accumulation after TNF-alpha stimulation occurred in a time- and dose-dependent fashion with a similar inhibition of PG accumulation after Dex exposure. To be certain that TNF-alpha stimulated PGE2 production was, indeed, a result of **COX-2** induction, RIAs were carried out with the **COX-2** -selective inhibitor NS-398. Cells stimulated with the NS-398 after TNF-alpha exposure demonstrated suppression of TNF-alpha-stimulated PGE2 formation. The results suggest that TNF-alpha elicits part of its pathophysiologic effects in preterm labour via alterations in **COX -2** gene expression within the placental microenvironment.

AN 97435415 MEDLINE
DN 97435415 PubMed ID: 9290146
TI Tumour necrosis factor-alpha induces cyclo-oxygenase-2 gene expression in first trimester trophoblasts: suppression by glucocorticoids and NSAIDs.
AU Imseis H M; Zimmerman P D; Samuels P; Kniss D A
CS Department of Obstetrics and Gynecology, Ohio State University, College of Medicine, Columbus, USA.
NC HD28360 (NICHD)
SO PLACENTA, (1997 Sep) 18 (7) 521-6.
Journal code: PMN; 8006349. ISSN: 0143-4004.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
ED Entered STN: 19971024
Last Updated on STN: 19971024
Entered Medline: 19971015